Is Coronary Artery Bypass Graft Operation in 48 Hours Following Carotid Stenting Safe?

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Objective: The purpose of this study was to assess the safety and effectiveness of the outcome of coronary artery bypass graft operation (CABG-O) in 48 hours following carotid artery stenting (CAS).

Materials and Methods: We report the results of a retrospective, single-center study designed to evaluate the feasibility and safety of CAS before cardiac surgery in neurologically symptomatic or asymptomatic patients. Twenty-three patients to whom CAS was applied because of symptomatic or asymptomatic carotid vascular stenosis were included in the study. CAS was accomplished in all patients without any complication. The mean time from CAS to CABG-O was 15.7±7 hours (range 8-48 hours). All patients were followed up for 19 months (range 9-47 months) for any adverse events such as stroke, acute myocardial infarction (AMI), stent restenosis and death.

Results: Most patients with carotid artery lesion were asymptomatic (82.6%). Stroke and AMI did not occur in any CAS patients during the procedure and the time interval between CAS and CABG-O. Major stroke was observed in one patient at the arm of CAS, on the first day postoperatively.

Conclusion: CABG-O in 48 hours following CAS is safe and not related to increasing the rate of AMI, stroke and death in 19 months of follow up.

Key words: Carotid artery disease, carotid artery stenting, coronary artery bypass graft operation

Introduction

The incidence of significant carotid artery disease in patients who undergo coronary artery bypass grafting operation (CABG-O) ranges from 3-22% (1, 2). This association increases the risk of stroke after CABG-O by 3 fold (3). At the present time, it is accepted that the main treatment position is carotid artery endarterectomy (CAE) for preventing the strokes and deaths due to carotid artery stenosis (4). Several therapeutic options exist for patients with combined carotid vascular disease and coronary artery disease: CABG-O alone, staged CE, and CABG-O (CABG-O applied a few days or a few weeks after CAE), reversed staged CAE, combined procedure (firstly CAE, then CABG-O at the same anesthesia session), staged carotid artery stenting (CAS) and CABG-O, reversed staged CAS and combined procedure during the same anesthesia (5). It was shown that postoperative mortality and morbidity risk increases with the synchronized surgical approach (6). However, in the staged surgical approach, while stroke rate decreases after CAE, the risk of acute myocardial infarction (AMI) increases during CAE and in the waiting period of CABG-O (7).

Recently, staged CAS, which is done by using distal cerebral emboli protection devices (DECPD) for high-risk patients, is suggested as a less invasive and newer method than CAE (8). Concern is felt that perioperative bleeding may occur because of double antiplatelet treatment (clopidogrel 75 mg and 300 mg aspirin daily) which is applied...
for protection from stent thrombosis after staged CAS (9). The wait-
ing time between CAS and CABG-O is more risky for the unstable
patients. The waiting time between CAS and CABG-O will be sig-
ificantly determined by the severity of the coronary artery disease.
However, very little data is available in the literature describing ca-
rotid stenting followed by staged CABG-O and the results are quite
different. The aim of our study is to evaluate the safety and effec-
tiveness of CABG-O following coronary artery stenting in 48 hours.

Materials and Methods

Clinical and procedural data was collected retrospectively from the
hospital’s electronic medical records. Carotid duplex ultrasonogra-
phy (Toshiba nemio XG) was done in all patients before CABG-O.
Patients with critical carotid stenosis on duplex ultrasonography
underwent diagnostic carotid angiography to confirm the degree
of stenosis before CAS. The severity of carotid vascular disease was
determined by the specialists of cardiovascular surgeon, interven-
tional radiologist and interventional cardiologist. It was thought ca-
rotid artery lesion is important if it’s diameter was >70% in sym-
tomatic patients and >80% in asymptomatic patients according to
North American Symptomatic Carotid Endarterectomy Trial crite-
rion (NASCET) (10). Carotid angiography and CAS was performed
by the same interventional radiologist. Patients were considered symptomat ic if an ipsilateral cerebrovascular event had occurred
within the last 4 months. Minor stroke is described as new devel-
oped neurological deficit that lasts longer than 24 hours shorter
than 7 days. Major stroke is described as new developed stroke that
lasts longer than 7 days; fatal stroke during CAS and later than CAS
is described as the death depending upon hemorrhagic or ischemic
stroke. Cardio-cerebrovascular early mortality was defined as
death related to a cardiac or cerebrovascular event into 30 day after
CABG-O. The patient was consultated by neurologist if there was
any clinical suspicion of neurological deficit during in CAS, the
period after the CABG-O. The patient was consultated by neurologist if there was
any clinical suspicion of neurological deficit during in CAS, the
time interval between CAS and CABG-O and the time of follow up after the CABG-O.

CAE was preferred in patients with angiographically visible thorn-
bus within the lesion, absence of femoral arterial access, intra-cra-
nial stenosis exceeding the severity of the extra-cranial stenosis,
severe proximal carotid artery tortuosity and severe preexistent
neurological disability.

Carotid Artery Stenting Technique: 300mg aspirin and 300 mg
clopidogrel were given before CAS and 70 IU/kg unfractional
heparin was given intravenously shortly before the procedure.
100 mg aspirin and 75 mg klopidogrel were given daily until the
CABG-O. Unfractionated Heparin was given intravenously as the
target activated clotting time of 200 to 250 s during CAS and aPTT
50-70 s during waiting time before CAS and CABG-O. CAS pro-
cedure was carried out with the guidance of digital subtraction
angiography (DSA) device (Philips Integris). Vascular attempt was
performed under local anesthesia with 7F long intraducer sheath
(Super Arrow-Flex, Arrow International, and Reading, PA, USA)
through femoral artery. Existing stenosis was confirmed by mak-
ing aortic arch and selective angiography of its divisions. Cerebral
circulation was evaluated, particularly Willus polygon. Long vas-
cular sheath was placed to ipsilateral main carotid with lesion.
DSEPD (SPIDER, eV3 Inc, Plymouth, Minnesota) was appealed
to the established distal of carotid artery stenosis at subpetrous
segment of internal carotid artery after passing with hydrophilic
coated 0.014 inch micro guide chorda (Transder, Target Thera-
peutics, Boston Scientific, Fremont, CA). Nitinol tapered stent
(The Protege @RX Carotid Stent System, eV3), which extends it-
self at stenosis level, was placed. Post stent dilatation procedure
was carried out with angioplasty balloons (Ultra soft PTA balloon
cath; Boston Scientific) which are appropriate to internal carotid
artery diameter after stenting. At control angiography, if residual
stenos is was %30 and beneath it at stenosis area or the area af-
ter stenosis, it was accepted as a success. If the residual stenosis
was over %30, it was redilated with appropriate balloon choice.
Control carotid and cerebral angiography was taken after balloon
dilatation. The procedure was ended by collecting filter.

CABG-O: Eligibility for CABG was evaluated by an invasive car-
diologist and cardiovascular surgeon based on standard AHA/ACC
guidelines (11). All patients were operated on by the same surgery
and anesthesia teams with the techniques of median sternotomy,
ascending aorta, right atrial cannulation, anterograde blood ca-
dioplegia and single cross clamp. Cardiopulmonary bypass(CPB)
was performed when APTT>400 seconds by giving 300 IU/kg un-
fractional heparin. During CPB, mean arterial pressure was 60-80
mm-Hg, perfusion pressure was 2.2 lt/minutes/m² and body tem-
perature was 32 degrees. After CPB, it was antagonized at the rate
of 1mg unfractional heparin /1 mg protamine sulphate.

Follow-up: Double anti-platelet treatment, which started at postop-
erative first day, was prolonged for 30 days. Re-operation, duration of exhu-
tation (hours), length of intensive care unit stay (days), dura-
tion of discharge (days) and death were followed up. All clinical
endpoints were described at the time of discharge from our institu-
tion. After CABG-O, all patients were followed up by the hospital’s
outpatient clinic (sequentially first week, first, 3 and 6 months, and
after 1 year). Over 1 year, mild and long- term follow-up were con-
ducted by telephone interview. Patients and their family members
were informed about our different treatment methods and the im-
portance of communication.

Exclusion criteria: The exclusion criteria were as follows severe
renal impairment (serum creatinine >2.3 mol/l), peripheral vascu-
lar disease that disabled femoral artery access, major stroke, or any
other illness that impeded their ability to provide informed con-
sent. Patients with chronic total occlusions, and long preocclusive
lesions (“string sign” lesions) were also excluded.

Statistical analysis

All analysis were performed using the SPSS (SPSS for Windows
15.0) software package. Continuous variables were presented as
mean±standard deviation. Categorical variables were presented as
the percentage. A value of P<0.05 was considered statistically sig-
nificant.

Study limitations

The main limitation of our study was the small sample size. A small
sample size can result in a low statistical power for equivalency
testing, leading to false-negative results. However, establishing this
population is very difficult and CAS is not a frequent procedure.
Another limitation of the study was its retrospective nature and the
need to rely on previous patient records during such studies. This
sample population is therefore a non-randomized partially selected group that will bias the outcome assessment to a degree.

Results

A total of 169 patients with significant or trivial carotid vascular disease were diagnosed through duplex ultrasonography. 30 patients had undergone carotid artery angiography for confirmation of severity of carotid vascular disease before CABG-O between July 2007 and May 2011. Of these patients, serious carotid vascular disease was not detected in three patients, two patients were unwilling to undergo CAS, abnormal anatomy in the aortic arch was present in two patients, femoral arterial access was not suitable for two patients because of serious iliac artery stenosis.

Twenty-three patients (Twenty-one patients with CAS, one patient with subclavian artery stenosis and one patient with vertebral artery stenosis) were included in the study. The mean age was 70.9±6.28 (range 61-79). Stent was successfully implanted in the carotid artery in all patients. Bilateral severe carotid vascular disease and coronary artery disease were detected in one patient who was had initially undergone CABG-O following unilateral CAS then underwent CAS for opposite carotid artery lesion one month after CABG-O. Demographic characteristics of patients are shown in Table 1. The time interval between the CAS and CABG-O was 15.7±7.19 hours (range 8-48 hours). The time interval between CAS and CABG-O was primarily determined by the cardiac surgeon according to stability of the patients. Stroke, AMI or death was not seen during the waiting time between CAS to CABG-O. Clinical characteristics and cardiac surgery results was shown in Table 2.

Table 1. Demographic characteristics of the patients

<table>
<thead>
<tr>
<th>Age</th>
<th>70.9±6.28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender: Male (n=16)</td>
<td>69%</td>
</tr>
<tr>
<td>Valvular heart disease(Aortic Valve replacement) (n=1)</td>
<td>4.32%</td>
</tr>
<tr>
<td>Hypertension (n=13)</td>
<td>56.5%</td>
</tr>
<tr>
<td>Diabetes mellitus (n=11)</td>
<td>52.2%</td>
</tr>
<tr>
<td>Hyperlipidemia (n=15)</td>
<td>65.2%</td>
</tr>
<tr>
<td>Smoking (n=17)</td>
<td>73.9%</td>
</tr>
<tr>
<td>Previous stroke history (n=2)</td>
<td>8.69%</td>
</tr>
<tr>
<td>Unstable angina pectoris (n=8)</td>
<td>34.3%</td>
</tr>
<tr>
<td>Angina on exertion (n=9)</td>
<td>39.2%</td>
</tr>
<tr>
<td>Serious left main coronary artery disease or equivalent (n=6)</td>
<td>26.5%</td>
</tr>
<tr>
<td>Symptomatic CVD (n=4)</td>
<td>17.2%</td>
</tr>
<tr>
<td>Previous minor stroke (n=4)</td>
<td>17.2%</td>
</tr>
<tr>
<td>Previous CEA (n)</td>
<td>-0-</td>
</tr>
<tr>
<td>Previous carotid angioplasty (n)</td>
<td>-0-</td>
</tr>
<tr>
<td>Previous CABG-O (n=1)</td>
<td>4.32</td>
</tr>
</tbody>
</table>

CABG-O: Coronary Artery Bypass Graft Operation, CAE: Carotid Artery Endarterectomy, CVD: Carotid Vascular Disease

Table 2. Clinical characteristics, cardiac surgery results and follow up

| Left ventricle ejection fraction | 48.0±4.89 |
| Left internal carotid artery stenting (n=12) | 52.1% |
| Right internal carotid artery stenting (n=9) | 39.1% |
| Left subclavian artery stenting (n=1) | 4.34% |
| Vertebral artery stenting (n=1) | 4.34% |
| Stenosis between 50-70% at contralateral carotid (n=4) | 17.9% |
| Severity of lesion in contralateral carotid >70% (n=1) | 4.34% |
| Waiting period after carotid artery stenting (hours) | 15.78±7.19 |
| Cardiopulmonary bypass time(minute) | 59.5±21.23 |
| Cross clamp time (minute) | 50.0±10.83 |
| Stroke after open heart surgery (hours) | 1 (4.34%) |
| Mean ventilation time (hours) | 6.4±0.29 |
| Length of intensive care unit stay (days) | 1.5±0.72 |
| Postoperative discharge time (days) | 6.0±2.08 |
| Mean follow-up time after CABG (months) | 18.7±7.32 |

CABG-O: Coronary Artery Bypass Graft Operation

Discussion

Stent endothelialisation is a slow process and is known to take about from 28 to 96 days to complete (12). Additionally, it has been known that stent restenosis can occur more frequently during the early period following CAS if sufficient antiplatelet agents are not given during the CAS procedure and interval period (13). However, antiplatelet agents used for stent endothelialisation can create concern about the risk of postoperative bleeding. Because of concern about bleeding, some writers suggest urgent CABG-O together with heparin and aspirin for avoiding the risk of postoperative bleeding due to clopidogrel and aspirin given as double antiplatelet treatment at the time of CAS (14). However, other writers suggest using short-acting glycoprotein IIa/IIIb inhibitors during CAS and discontinuing them 4-6 hours before CABG-O (14). In this short waiting period, we performed CAS by using heparin, aspirin and clopidogrel in all patients in our study and gave heparin infusion to maintain an activated clotting time of 200 to 250 s during CAS and aPTT 50-70 s from CAS up to CABG-O.
As a result of our study, re-operation because of bleeding was not necessary.

Bradycardia and hypotension can occur during CAS and this situation can last for a few days or weeks (15). In this period, this can cause strokes in the common atherosclerotic cerebral circulation or to AMI in the patients who have a serious coronary lesion. Therefore, to take the patients with serious coronary artery lesion, for urgent CABB-G after CAS can be effective in reducing AMI and cerebral stroke rates which are seen during the interval period. It was reported in previous studies that AMI occurred in 5.8% of patients who were treated with a staged operation prior to CABG-O (5). Additionally, Yuki Okamoto et al. (16) reported in a study including 20 patients that one patient was taken to urgent CABB-G due to AMI in the 30 days waiting period. Lopes et al. (17) observed 49 patients retrospectively who were taken to CABB-G after the 15 days from CAS. They reported that minor stroke occurred in 3 patients during the 15 days waiting period and 3 patients died because of cardiac events. In contrast to these studies, there was a short waiting period in our study. During the short waiting period it was observed that no TIA and stroke, or death occurred. Our strategy may have some additional advantages as compared with staged CAS-CABG approaches, by reducing the risk of acute myocardial infarction in the time elapsing between the two procedures, as the interval between them is virtually eliminated.

In a study published by Guzman LA et al. (18) they documented that carotid revascularization by means of CAS before CABG carries an elevated incidence of death and stroke. In this study, the shortest mean waiting period was 15 days and the longest 69 days. During this period, a total of 6 (2.2%) patients died and all deaths were considered cardiac-related events. Moreover they reported that the total stroke rate was 6.1% in a postoperative period. Jan Van der Heyden et al. (19) reported in a study including 57 patients, who underwent CAS due to serious symptomatic carotid vascular disease, that AMI occurred in 1 patient in the waiting period of 28 days after CAS and stroke occurred in 4 patients (ipsilateral with the CAS in 3 patients, contra lateral in 1 patient). They also reported that the rate of CAS and postoperative 30 days total stroke was 8.8%; the rate of combined stroke, death and AMI was 12.3%. However, the rate of combined stroke, death and AMI was 4.3% in our study. Moreover, stroke and stent restenosis were not seen during 19.7±6.9 months (range, 9-47 months) follow-up in our study. We think that the probable reason for having fewer severe neurological incidents in our study may be the short waiting period and double antiplatelet treatment (100 mg aspirin and 75 mg clopidogrel daily) which started at postoperative first day.

Conclusion

This study shows that AMI, stroke and death rates are decreased by CAS followed by CABB-O in 48 hours during the preoperative time interval, intraoperative and postoperative follow up.

Consequently CAS followed by CABB-O in 48 hours can provide a valuable treatment for patients with combined carotid and critically obstructive coronary disease. Our findings should be supported by studies which have larger series and control groups, including the long term results.


