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Management of Carotid Artery Disease in the Setting of Coronary Artery Disease in Need of Coronary Artery Bypass Surgery

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1. Introduction

Coronary artery bypass graft surgery (CABG) is one of the most commonly performed major surgeries in the United States with over 397,000 CABG's performed in 2010.(Go, Mozaffarian et al. 2012) One of the most dreadful adverse sequelae of CABG is stroke which is also the 2nd most common major post-operative complication seen with CABG, occurring in 1 to 5% of patients.(Furlan, Sila et al. 1992; Brown, Kugelmass et al. 2008) Patients suffering from postoperative stroke have a very high incidence of in-hospital mortality.(Hogue, Murphy et al. 1999) Studies have shown that presence of extracranial carotid artery stenosis (ECAS) is a strong risk factor for post-operative morbidity and mortality due post-CABG strokes.(Brown, Kugelmass et al. 2008) In this book chapter, we will review the epidemiology of concomitant coronary and carotid artery disease, the association with post-operative stroke, recommendations for pre-operative ECAS screening and management options for patients in whom ECAS is identified.

Co-prevalence of carotid and coronary artery disease and its implications on perioperative and postoperative morbidity and mortality: Atherosclerosis is a systemic disease which is usually present in multiple vascular beds simultaneously.(Beique, Ali et al. 2006) In a recent study from the Cleveland Clinic involving 45,432 patient's, presence of carotid artery disease was confirmed as a significant risk factor for perioperative stroke after CABG. (Tarakji, Sabik et al. 2011) In the REACH Registry which was comprised of 67,888 patients, 10% of patients had concomitant coronary artery disease (CAD) and cerebrovascular disease (CVD). Anastasiasdis et al evaluated carotid arteries in 307 patients undergoing CABG and reported that while 3 out of 4 patients undergoing CABG had carotid atherosclerosis, the majority of these (63%) had <

50% ECAS. (Anastasiadis, Karamitsos et al. 2009). Various studies have reported the incidence of ECAS with varies degree of stenosis among the patient populations undergoing CABG which are summarized in table 1.

Study	Number of patients undergoing CABG being evaluated for ECAS	Prevalence of ECAS %
Wanamaker et al	559	ECAS >50% : 36%
Shirani et al	1045	ECAS > 60% : 6.9%
Anastasiadis et al	307	ECAS > 70% : 13%
Cornily et al	205	ECAS >70% : 5.8%
Salasidis et al	387	ECAS > 80% : 8.5%
Schwartz et al	582	ECAS > 50% : 22% ECAS > 80% : 12%

Abbreviations: CABG, coronary artery bypass grafting; ECAS, extracranial carotid artery stenosis.

Table 1. Prevalence of extracranial carotid artery stenosis among patients undergoing coronary artery bypass grafting.

Salasidis et al identified increasing age, history of previous carotid revascularization and presence of PAD in addition to severe ECAS as risk factors for neurological events after cardiac surgery, highlighting that ECAS is only 1 of a number of factors that drives peri-operative stroke risk.(Salasidis, Latter et al. 1995)

Interestingly, the likelihood of having ECAS increases with the underlying severity of CAD (Table 2).

Severity of CAD	Prevalence of Significant Carotid Atherosclerosis (%)
1- vessel CAD	5.3%
2- vessel CAD	13.5%
3- vessel CAD	24.5%
Left main disease	40%
3-vessel CAD or left main disease	24%

Table 2. Prevalence of significant carotid artery stenosis (extracranial carotid artery stenosis \geq 50%) among patients with different severity of coronary artery disease based on number of vessels involved or left main disease.

It was postulated that increasing degree of stenosis was associated with increased risk of perioperative stroke by Naylor et al who reported that among 5,453 patients undergoing CABG, the risk of perioperative stroke was <2%, 3%, 5% and 7-11% among patients who had < 50% ECAS, 50-99% unilateral ECAS, 50-99% bilateral ECAS and occluded carotid artery respectively.(Naylor, Mehta et al. 2002)

2. Screening for carotid artery disease

Screening for carotid artery disease is usually performed with carotid duplex ultrasound. Screening recommendations for carotid artery disease are somewhat controversial and vary across medical societies.(Goldstein, Adams et al. 2006; Bates, Babb et al. 2007; Qureshi, Alexandrov et al. 2007; 2008; Brott, Halperin et al. 2011) The most widely accepted multisocietal vascular practice guidelines involving 14 different vascular societies including the American College of Cardiology Foundation, American Heart Association Task Force on Practice Guidelines, the American Stroke Association, American Association of Neuroscience Nurses, American Association of Neurological Surgeons, American College of Radiology, American Society of Neuroradiology, Congress of Neurological Surgeons, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of NeuroInterventional Surgery, Society for Vascular Medicine, and Society for Vascular Surgery recommend screening for patients with carotid bruit or patients with CAD or symptomatic PAD or atherosclerotic aortic aneurysm as well those who may not have evidence of atherosclerosis but have 2 or more cardiovascular risk factors such as hypertension, dyslipidemia, tobacco smoking, family history of premature atherosclerosis or family history of ischemic stroke.(Brott, Halperin et al. 2011). The US Preventive Service Task Force recommended against screening as it was not cost-effective in asymptomatic patients.(Bates, Babb et al. 2007) The American Society of Neuroimaging recommended against the screening of unselected populations but advised the screening of adults older than 65 years of age who have 3 or more cardiovascular risk factors (Qureshi, Alexandrov et al. 2007)

For patients undergoing elective CABG, the multi-societal guidelines recommend screening for carotid artery disease in patients older than 65 years of age and in those with left main stenosis, PAD, history of cigarette smoking, history of stroke or TIA or carotid bruit. The American Heart Association and American College of Cardiology CABG guidelines offer recommendations consistent with the multi-societal vascular guidelines, however they also recommend that patients who have history of hypertension or diabetes mellitus also undergo preoperative carotid duplex scanning.(Hillis, Smith et al. 2011)

3. Utility of advanced imaging carotid artery beyond carotid duplex ultrasound

Duplex ultrasound is an excellent tool to diagnose ECAS.(Eagle, Guyton et al. 1999) However there are certain inherent errors that can occur with duplex. The presence of calcification at the site of stenosis may cause underestimation of degree of stenosis; similarly contralateral occlusion may lead to falsely elevated velocities in the ipsilateral carotid artery leading to overestimation of the degree of stenosis. (Mitchell E 2004) In such situations additional imaging with computed tomography angiography (CTA) or magnetic resonance angiography (MRA) may further characterize the degree of stenosis as well as provide insight on plaque charac-

teristics, aortic pathology and intracranial ICA abnormalities. Given the excellent images rendered by CTA or MRA, conventional angiography is rarely required for determining degree of stenosis among those with normal or minimally impaired renal function. For those with moderate to severe chronic kidney disease, MRI may be relatively contraindicated due to the risk of nephrogenic systemic sclerosis and invasive angiography favored over CTA given its lower relative contrast volume and risk of contrast-induced acute kidney injury.

Other factors that may lead to increased stroke risk beyond degree of stenosis, including cerebrovascular reserve (CVR). Severe ECAS reduces cerebral perfusion pressure. Autoregulation of the cerebral vasculature dilates the cerebral arterioles maximally, and with further reduction in cerebral perfusion, blood flow will eventually decrease, causing impairment in cerebral perfusion leading to stroke. CVR can be assessed by two approaches. The first, CVR can be determined through direct measurements of brain tissue with flow-sensitive imaging through positron emission tomography, CT perfusion or MR perfusion before and after vasodilator stimulation. A second, indirect approach utilizes transcranial Doppler to assess flow velocities distal to the lesion, typically in the middle cerebral artery before and after vasodilatory stimulation, with increase in flow velocities used to indirectly measure CVR. (Gupta, Chazen et al. 2012) In a meta-analysis of patients with severe ECAS, there was an association between impaired CVR and increased stroke risk. (Gupta, Chazen et al. 2012) An incomplete circle of Willis has also been associated with increased ipsilateral cerebral ischemia during carotid cross clamping with CEA. (Manninen, Makinen et al. 2009) and as a risk factor for ischemic stroke (Hoksbergen AW et al. *Cerebrovasc Dz* 2003;16:191-8) Current guidelines do not comment on use of cerebral perfusion imaging when assessing stroke risk due to insufficient evidence available so far. (Brott, Halperin et al. 2011; Hillis, Smith et al. 2011)

4. Treatment

Treatment options for ECAS consist of medical therapy and in some cases, revascularization.

Medical therapy for carotid artery disease: Medical therapy is the cornerstone of treatment for atherosclerotic disease. Medical therapy for ECAS comprises of treatment of risk factors such as hypertension, dyslipidemia, diabetes mellitus, and tobacco use and use of antiplatelet therapy. Consensus societal class I recommendations for treatment of atherosclerotic carotid artery disease appear in Table 1 (Brott, Halperin et al. 2011).

Treatment of hypertension: Hypertension increases risk of stroke significantly. For each 10 mm Hg rise in blood pressure, the stroke risk increases by 30 to 45%. This risk significantly is significantly reduced with antihypertensive therapy. A systemic review of 7 randomized controlled trials (RCT) showed that treatment with antihypertensive agents reduced the risk of recurrent stroke by 24%. A meta-analysis of 40 studies with > 188,000 patients reported a 33% decreased risk of stroke with a 10 mm Hg reduction in BP. (Lawes, Bennett et al. 2004; Brott, Halperin et al. 2011) Hypertension should be treated to maintain a goal blood pressure (BP) < 140/90 mm Hg for all patients with ECAS except those with diabetes mellitus (DM) and chronic

Recommendation	Class of Indication	Level of Evidence
Antihypertensive treatment is recommended for patients with hypertension and asymptomatic extracranial carotid or vertebral atherosclerosis to maintain blood pressure below 140/90 mm Hg	I	A
Treatment with a statin medication is recommended for all patients with extracranial carotid or vertebral atherosclerosis to reduce low-density lipoprotein (LDL) cholesterol below 100 mg/dL	I	B
Patients with extracranial carotid or vertebral atherosclerosis who smoke cigarettes should be advised to quit smoking and offered smoking cessation interventions to reduce the risks of atherosclerosis progression and stroke	I	B
Antiplatelet therapy with aspirin, 75 to 325 mg daily, is recommended for patients with obstructive or nonobstructive atherosclerosis that involves the extracranial carotid and/or vertebral arteries for prevention of MI and other ischemic cardiovascular events, although the benefit has not been established for prevention of stroke in asymptomatic patients	I	A
In patients with obstructive or nonobstructive extracranial carotid or vertebral atherosclerosis who have sustained ischemic stroke or TIA, antiplatelet therapy with aspirin alone (75 to 325 mg daily), clopidogrel alone (75 mg daily), or the combination of aspirin plus extended-release dipyridamole (25 and 200 mg twice daily, respectively) is recommended (<i>Level of Evidence: B</i>) and preferred over the combination of aspirin with clopidogrel	I	B
Aspirin (81 to 325 mg daily) is recommended before CEA and may be continued indefinitely postoperatively	I	A
Beyond the first month after CEA, aspirin (75 to 325 mg daily), clopidogrel (75 mg daily), or the combination of low-dose aspirin plus extended-release dipyridamole (25 and 200 mg twice daily, respectively) should be administered for long-term prophylaxis against ischemic cardiovascular events	I	B
Administration of antihypertensive medication is recommended as needed to control blood pressure before and after CEA.	I	C
The findings on clinical neurological examination should be documented within 24 hours before and after CEA.	I	C
Before and for a minimum of 30 days after CAS, dual-antiplatelet therapy with aspirin (81 to 325 mg daily) plus clopidogrel (75 mg daily) is recommended. For patients intolerant of clopidogrel, ticlopidine (250 mg twice daily) may be substituted.	I	C
Administration of antihypertensive medication is recommended to control blood pressure before and after CAS.	I	C

Table 3. Recommendations from multisocietal guidelines for extracranial carotid artery stenosis.

kidney disease (CKD) in whom goal BP is < 130/80 mm Hg. (Chobanian, Bakris et al. 2003). These guidelines are applicable to all patients except those in the hyperacute period after stroke. The type of agent utilized should be based on presence of other co-morbid conditions (e.g., diabetes, CKD, CAD, etc.) and not on presence of carotid disease. (Chobanian, Bakris et al. 2003).

Management of Diabetes Mellitus: Presence of diabetes mellitus is associated with increased stroke risk. In the Rotterdam study, diabetes was the only risk factor independently associated with severe progression of carotid stenosis. (van der Meer, Iglesias del Sol et al. 2003). Although glycemic control is necessary, intensive control may not be of incremental benefit. In the UKPDS study, intensive glucose control compared to conventional glucose control did not reduce stroke risk. Similarly, in the ACCORD and ADVANCE trials, intensive glucose control to lower hemoglobin A1c <6 or <6.5, respectively, did not reduce stroke risk when compared to conventional treatment. (Gerstein, Miller et al. 2008; Patel, MacMahon et al. 2008) Intensive control of other risk factors in patients with diabetes is also beneficial, such as administering statins in patients with diabetes even with 'normal' serum cholesterol. Doing so may lower the risk of stroke by as much as 48%. (Colhoun, Betteridge et al. 2004). All diabetic patients with atherosclerotic ECAS should be treated with diet, exercise and glucose lowering drugs as needed to maintain hemoglobin A1c <7. All patients should be treated with statins regardless of cholesterol levels and LDL cholesterol goal should be < 100mg/dl. (Brott, Halperin et al. 2011)

Treatment of dyslipidemia: Dyslipidemia isn't as strongly associated with ischemic stroke as hypertension or diabetes mellitus. In the MR-FIT trial which involved over 350,000 men, the relative risk of death was 2.5 times higher in men with highest vs. the lowest cholesterol levels. (Iso, Jacobs et al. 1989) In the ARIC study, dyslipidemia weakly correlated with ischemic stroke. (Shahar, Chambless et al. 2003); however in the Women's Health Study which evaluated over 27,000 women, total and LDL cholesterol were associated with increased risk of stroke. (Kurth, Everett et al. 2007). The lipid lowering agents of choice are the statins which in addition to lowering cholesterol, work through so-called provide pleotropic effects such as plaque stabilization and reduction in inflammation which may help reduce overall cardiovascular events. A metaanalysis comprising of 26 trials with > 90,000 patients found that statins reduce stroke risk by 21%; With every 10% reduction of serum LDL cholesterol, there was a 15.6% reduction in stroke. (Amarenco, Labreuche et al. 2004). The SPARCL trial randomized patients with recent stroke or TIA to atorvastatin 80 mg daily or placebo and found that atorvastatin reduced the incidence of ischemic stroke by 22%. (Amarenco, Bogousslavsky et al. 2006) All patients with atherosclerotic carotid artery disease should be treated with statin to maintain an LDL cholesterol < 100 mg/dl and it is reasonable to maintain LDL cholesterol < 70 mg/dl, especially in high risk patients such as those with ECAS and one or more cardiac risk factors such as current smoker or diabetes mellitus. If the goal LDL cholesterol is not achieved with statin therapy, other lipid lowering agents such as bile acid sequestrants, niacin or ezetimibe can be added to statin therapy. (Brott, Halperin et al. 2011)

Smoking Cessation: Smoking is strongly associated with increased stroke risk. Cigarette smoking is associated with 50% increase in relative risk of ischemic stroke. (Howard, Wagenknecht et al. 1998) Even patients who are past cigarette smokers have a 25% higher risk of stroke compared to lifelong non-smokers. (Howard, Wagenknecht et al. 1998) The Framingham

Heart Study and Cardiovascular Health Study both have reported an association between quantity and period of time an individual smoked and increased risk of stroke.(Tell, Rutan et al. 1994; Wilson, Hoeg et al. 1997). All smokers should be asked about smoking status on every visit and if currently smoking should be counseled on every visit. Every vascular specialist should assist these patients in developing a plan to quit smoking which would include behavioral and pharmacological interventions.(Rooke, Hirsch et al. 2012)

Antiplatelet therapy: Patients undergoing CABG should be on antiplatelet therapy regardless of the presence or absence of ECAS. The benefits of antiplatelet therapy are well-defined in patients with symptomatic ECAS. (2002), and it appears that clopidogrel is superior to aspirin in preventing death, MI or stroke among those with a history of PAD (CAPRIE PAD subgroup analysis/paper). The benefit of dual antiplatelet therapy over monotherapy in this sub-group of patients is not as well-defined and was not proven in the MATCH or in the overall CHARISMA trial.(Diener, Bogousslavsky et al. 2004; Bhatt, Fox et al. 2006) However, in the CHARISMA trial, dual antiplatelet therapy with aspirin and clopidogrel did reduce the incidence of death, MI or stroke among those with established atherosclerotic vascular disease at baseline.(Bhatt, Fox et al. 2006). The ESPS-2 trial demonstrated that extended-release dipyridamale 200 mg twice daily along with aspirin 25 mg once daily (aggrenox) was superior to aspirin alone in secondary prevention of ischemic strokes.(Diener, Cunha et al. 1996) The PROFESS trial compared aggrenox to clopidogrel for secondary prevention of ischemic stroke and found no difference in recurrent stroke reduction in both groups.(Sacco, Diener et al. 2008). Anticoagulant therapy was evaluated in the WARSS study where aspirin was compared to warfarin for stroke prevention in patients with recent stroke, No added benefit was observed with warfarin compared to aspirin in patients with large-vessel atherosclerosis.(Mohr, Thompson et al. 2001). Patients undergoing CABG who have atherosclerotic ECAS will benefit from antiplatelet monotherapy with at aspirin at a minimum; whether dual antiplatelet therapy is incrementally beneficial is less well established.

In summary, it is recommended that all patients with ECAS, regardless of whether they are to undergo CABG receive aggressive risk factor modification in addition to statins, beta-blockers, angiotensin converting enzyme inhibitors or angiotensin receptor blockers and antiplatelet therapy unless contraindicated.

Revascularization: The overall goal of carotid artery revascularization is to reduce the incidence of stroke beyond that afforded by medical therapy alone. In the perioperative setting, the decision about whether to perform carotid artery revascularization, which revascularization modality to pursue and when to revascularize (e.g., CEA or CAS preceded by CABG, CABG preceded by CEA or CAS, concomitant CEA or CAS at the time of CABG). remain challenging.

Indications for carotid revascularization: The decision to revascularize the carotid artery hinges on the presence or absence of symptoms attributable to ECAS, degree of ECAS and urgency of CABG.

The current multisocietal vascular guidelines recommend that carotid revascularization by CEA or CAS with embolic protection before or concurrent with myocardial revascularization

surgery is reasonable in patients with greater than 80% carotid stenosis who have experienced ipsilateral retinal or hemispheric cerebral ischemic symptoms within 6 months. They also state that in patients with asymptomatic carotid stenosis, even if severe, the safety and efficacy of carotid revascularization before or concurrent with myocardial revascularization are not well established..(Brott, Halperin et al. 2011)

The American College of Cardiology and American Heart Association CABG guidelines state that is reasonable to revascularize ECAS of 50-99% in patients with previous history of stroke or TIA and In those who do not have a prior history of stroke or TIA, they consider it reasonable to revascularize especially in the setting of bilateral ECAS of 70-99% or unilateral ECAS of 70-99% with contralateral occlusion. (Hillis, Smith et al. 2011)

In addition to it is necessary to identify and appropriately treat other factors such as atrial fibrillation, low output cardiac state, aortic arch atheroma, age, diabetes etc which also increase the risk for perioperative stroke.

Strategies for carotid revascularization in patients undergoing CABG:

The 2 revascularization modalities most commonly used are CEA and carotid stenting. Both of these modalities are approved by the Food and Drug Administration (FDA) for carotid revascularization. (FDA 2011)

Carotid endarterectomy: CEA has proven to be beneficial in stroke reduction in patients with symptomatic and asymptomatic ECAS.(1991; 1991; 1995; 1996; 1998; Barnett, Taylor et al. 1998; Halliday, Mansfield et al. 2004; Halliday, Harrison et al. 2010)

There are three surgical strategies for carotid revascularization in patients undergoing CABG:

Concomitant CEA-CABG: CEA is performed prior CABG under the same anesthesia.

"Staged CEA- CABG": CEA is performed prior to CABG in different settings. Patient is initially scheduled for CEA and then later for CABG,

"Reverse staged": Here CABG is initially performed and then CEA is scheduled at a later date or time.

A meta-analysis of 56 reports comparing these 3 surgical strategies showed higher rates of stroke in patients undergoing reverse staged procedures (10%) as compared to concomitant (6%) and staged procedures (5%) However, staged procedures had the highest rates of perioperative MI (11%[p=0.01]) and death (9%[p=0.02]) compared to concomitant(5% & 6%) and reverse staged procedures (3% and 4%).(Moore, Barnett et al. 1995) Another meta-analysis of 16 studies with over 800 concomitant and 920 staged procedures showed an increased risk of composite endpoint of stroke or death among patients undergoing combined procedure compared to staged procedures (9.5% v 5.7%; relative risk 1.49; 95% confidence interval 1.03-2.15; p = 0.034).(Borger, Fremes et al. 1999) Naylor et al performed a systematic review comparing outcomes following staged or concomitant procedures which included 94 studies with concomitant procedures and 24 studies with staged procedures.(Naylor, Cuffe et al. 2003) 60% of the patients in these studies were asymptomatic. Bilateral 50-99% ECAS or carotid occlusion was present in 30-37% of the patients. Thirty nine % of patient who underwent

concomitant were labeled as having "urgent" surgery, 72% of them were classified as having New York Heart Association grade 3 or 4 and 25% of patients had left main disease.(Naylor, Cuffe et al. 2003) It was noted that mortality was highest among the patients undergoing concomitant (4.6%, 95% CI 4.1-5.2) and death \pm stroke rate was also higher compared to other staged procedure (8.7%, 95% CI 7.7-9.8). Reverse staged procedures had the highest risk of ipsilateral stroke (5.8%, 95% CI 0.0-14.3) and any stroke (6.3%, 95% CI 1.0-11.7) but with the lowest risk for peri-operative MI (0.9%, 95% CI 0.5-1.4). Staged procedures had the lowest rate of death \pm stroke (6.1%, 95% CI 2.9-9.3) but the highest rate of peri-operative MI (6.5%, 95% CI 3.2-9.7). However, the benefit seen with staged procedures on reduction in stroke and death was no longer significant when peri-operative MI was also included in the combined outcomes. The risk of death/stroke/ MI was 11.5% (95% CI 10.1-12.9) following concomitant procedures versus 10.2% (95% CI 7.4-13.1) after staged procedures. Non of these studies had randomized patients to the different strategies and hence may have selection bias.

Carotid Artery Stenting: Randomized clinical trials have shown that carotid stenting is an effective method of revascularization equivalent to carotid endarterectomy.(Yadav, Wholey et al. 2004; Brott, Hobson et al. 2010) The protected carotid-artery stenting versus endarterectomy in high-risk patients (SAFFIRE) trial proved efficacy of carotid stenting. It consisted of patients at high surgical risk who were randomized to carotid stenting with embolic protection device or carotid endarterectomy. The study proved that carotid stenting was non-inferior to CEA (cumulative incidence, 20.1 percent; absolute difference, -7.9 percentage points; 95 percent confidence interval, -16.4 to 0.7 percentage points; $P=0.004$ for noninferiority, and $P=0.053$ for superiority). (Massop, Dave et al. 2009) Sixteen percent of patients in the SAFFIRE trial had severe CAD too. In the Stenting versus Endarterectomy for Treatment of Carotid-Artery Stenosis (CREST) trial, 2502 patients with indication for carotid revascularization were randomized to carotid stenting or CEA regardless of level of surgical risk. The CREST showed that CAS had similar adverse outcomes as CEA proving it to be equivalent to CEA for revascularization (7.2% and 6.8%, respectively; hazard ratio with stenting, 1.11; 95% confidence interval, 0.81 to 1.51; $P=0.51$). (Brott, Hobson et al. 2010).

Three different strategies can be utilized when carotid stenting is performed in patients undergoing CABG:

1. "Staged": CAS followed by CABG (CABG is done weeks later after CAS)
2. "Same day hybrid": CAS followed by CABG on the same day.
3. Concomitant ("true hybrid"): CAS followed by CABG on the same day in the same OR done immediately after CAS is completed.

In the staged method after carotid stenting, patients are treated with dual antiplatelet therapy with aspirin and clopidogrel for a few weeks (most commonly 4 weeks). Later, clopidogrel is held for 5-7 days prior to CABG. Patients undergoing hybrid procedures (true or same day) are placed on heparin between procedures and later on clopidogrel as soon as possible after CABG.

Mendiz et al reported 30 high surgical risk patients for CEA who underwent synchronous CAS then CABG and/or valve surgery. Among these patients, 1 patient had TIA and no patients suffered stroke or MI.(Mendiz, Fava et al. 2006) Versaci et al reported 101 patients who underwent CABG immediately after CAS. The 30-day composite incidence of disabling stroke, AMI or death was 4%: 2 patients had stroke after CAS. (Versaci, Reimers et al. 2009). Another series of 22 patients who underwent true hybrid procedure showed no deaths or MI and one case of contralateral stroke. There were no cases of major postoperative bleeding or stent thrombosis.(Palombo, Stella et al. 2009) Van der Heyden et al reported 356 patients with asymptomatic ECAS who underwent staged CAS - CABG with a mean interval of 22 days between the 2 procedures. The 30-day post-CABG stroke and death rate was 4.8%, MI was 2% and MI and death was 6.7%.(Van der Heyden, Suttorp et al. 2007) Naylor et al performed a meta-analysis of 11 studies involving 760 CAS plus CABG procedures.(Naylor, Mehta et al. 2009) Majority of the patients in this analysis were asymptomatic (87%) and majority had unilateral ECAS (82%). The study reported a mortality of 5.5% (95% confidence interval, CI: 3.4-7.6), ipsilateral stroke rate of 3.3% (95% CI: 1.6-5.1), all-cause stroke rate of 4.2% (95% CI: 2.4-6.1) and a MI rate of 1.8% (95% CI: 0.5-3.0) at 30-day follow-up. These results are comparable to systematic reviews of staged and concomitant carotid CEA-CABG, and suggest that staged CAS-CABG appears to as effective as staged CEA-CABG.

Decision regarding appropriate procedure and strategy for carotid revascularization in patients with undergoing CABG:

There are no randomized clinical trials comparing CAS and CEA in this patient group. Data from the Nationwide Inpatient Sample consisting of 27,084 patients who underwent carotid stenting before CABG or combined CEA - CABG surgery during the 5 years from 2000 to 2004 reported that 96.7% underwent CEA plus CABG surgery versus 3.3% who had carotid stenting plus CABG. Fewer perioperative strokes were reported among patients undergoing staged carotid stenting - CABG than among those undergoing staged CEA - CABG stroke (2.4% versus 3.9%). In this non-randomized data, patients undergoing staged CEA - CABG surgery faced a 62% greater risk of postoperative stroke than patients undergoing staged CAS-CABG surgery (OR 1.62, 95% CI 1.1 to 2.5; $p < 0.02$). (Timaran, Rosero et al. 2008) There was no difference in the combined risk of stroke and death between the treatment (OR 1.26, 95% CI 0.9 to 1.6; $p = \text{NS}$). (Timaran, Rosero et al. 2008) Another study compared hybrid CAS - CABG procedures ($n=56$) to concomitant CEA-CABG procedure ($n=111$). In this study patients undergoing CAS at baseline were more likely to have unstable/severe angina (52% vs 27%, $p = 0.002$), severe left ventricular dysfunction (20% vs. 9%, $p = 0.05$), symptomatic carotid disease (46% vs. 23%, $p = 0.002$), and the need for repeat open heart surgery (32% vs. 9%, $p = 0.0002$). Severe contralateral carotid disease was more prevalent in the concomitant CEA+CABG group (28% vs. 11%, $p = 0.01$). On 30-day follow-up, CAS group had a significantly lower incidence of stroke or MI (5% vs. 19%, $p = 0.02$). (Ziada, Yadav et al. 2005) Another study involving 659 patients in whom CEA-CABG, CAS-CABG (staged) or CAS-CABG (hybrid) was performed in 28.1%, 57.4% and 13.5% of patients respectively showed a 30-day compo-

site endpoint of death, MI and stroke of 4.8%, 2.4% and 8.6% respectively ($p=0.01$). (Ribichini, Tomai et al. 2010)

Timing of carotid revascularization when indicated is chosen based on symptoms status of the carotid and coronary territory, severity of carotid and coronary disease and level of expertise available at the institution. (Venkatachalam and Shishehbor 2011)

Symptomatic carotid artery disease with ECAS >50-99% stenosis:

1. Symptomatic carotid disease and asymptomatic coronary disease or stable angina: In these patients carotid revascularization should be pursued prior to CABG, staged carotid stenting then followed by 4 weeks of dual antiplatelet and then CABG or staged CEA - CABG or concomitant CEA-CABG is usually considered. Selection of patients for carotid stenting or CEA is based co-morbidities, anatomy and local expertise available.
2. Symptomatic carotid disease and symptomatic coronary disease (acute coronary syndromes): In these patients carotid disease should be revascularized initially or concomitantly. Concomitant CEA-CABG or "same day" or "true hybrid" stenting procedures are usually considered. In case need for emergent CABG's, reverse stages CABG-CEA procedures can be considered.

Asymptomatic carotid stenosis (ECAS > 80-99%) is further classified as high risk or low risk groups. High risk group consists of patients with bilateral ECAS > 80-99% or unilateral ECAS >80-99% with contralateral occlusion and asymptomatic ECAS 80-99% with impaired cerebral perfusion reserve. Patients without these features are considered low risk.

1. Asymptomatic ECAS with high risk features and symptomatic coronary disease (acute coronary syndromes): These patients are at high risk for myocardial infarction as well as stroke and hence should be considered for concomitant CEA-CABG or "same day" or "true hybrid" CAS-CABG.
2. Asymptomatic ECAS with high risk features with stable angina: These patients should be considered for staged CAS-CABG.
3. Asymptomatic ECAS with low risk features and stable angina or acute coronary syndromes: These patients should initially undergo coronary revascularization with carotid revascularization (stenting or CEA) at a later date on an elective basis.

5. Conclusion

To date, stroke remains one of the most devastating complications after open heart surgery with serious adverse economic, psychological and clinical implications on healthcare and individuals suffering from it. (Roach, Kanchuger et al. 1996; Hogue, Murphy et al. 1999) Identifying patients at risk of stroke after CABG and applying measures to reduce its occurrence are extremely vital.

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