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Synchronous carotid endaterectomy and coronary artery bypass grafting versus staged procedure in patients with severe carotid and coronary artery disease

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Abstract

Background: Atherosclerosis is a pathological process involving blood vessels all over the body in varying intensity. Occurrence of significant carotid artery disease in patients requiring coronary artery bypass grafting (CABG) results in a dilemma regarding the best surgical strategy for addressing both. Our objective was to compare the efficacy of synchronous carotid endarterectomy (CEA) and CABG with staged CEA followed by CABG.

Methods: During a four year period, from April 2013 to March 2017, 42 patients underwent CEA with CABG. Of these, 20 patients underwent synchronous procedure (group 1), and 22 underwent staged procedures (group 2) within 30 days apart.

Results: 42 patients underwent CEA with CABG either in synchronous or staged fashion. In synchronous group, 2 patients (10%) had stroke, 3 patients (15%) had reversible ischemic neurological deficit and 4 patients (20%) had convulsions. In the staged group, one patient (4.5%) required re-exploration for bleeding, one patient (4.5%) had stroke and one patient (4.5%) had convulsions. The result was found to be statistically significant on comparing group 1 with group 2.

Conclusion: Synchronous and staged procedures have their own merits and demerits. Patients with critically stenosed coronary and carotid artery lesions with accompanying severe comorbidities should preferably undergo synchronous procedures with CEA followed by CABG and staged procedures should be reserved for patients with chronic stable angina with lesser comorbidities.

Keywords: Synchronous and staged carotid endarterectomy with CABG, Carotid Artery Stenting

Introduction

Atherosclerosis is characterised by subendothelial lipid accumulation, scarring and inflammation in the arteries causing luminal stenosis, calcification or thrombosis.[1] Atherosclerosis is a systemic disease. Thus, coronary arteries and bilateral carotid arteries may be involved in the disease process in varying degrees. Significant luminal stenosis seen in coronary arteries results in myocardial infarction (MI) and its grave complications. Involvement of carotid arteries can cause transient ischemic attacks (TIA), stroke or rarely sudden death. Therefore, significant luminal stenosis of both puts the patient under higher risk due to challenges in adopting the ideal surgical strategy. 28% of patients

with carotid artery stenosis requiring carotid endarterectomy (CEA) have significant coronary artery disease; 12% of patients undergoing myocardial revascularization have significant carotid artery stenosis.[2]

The surgical management of both carotid and coronary artery disease has been a constant challenge to clinicians for decades. These patients with advanced atherosclerosis may have left main coronary artery (LMCA) disease and low ejection fraction to complicate things further.[3] They are at an increased risk for developing stroke during coronary artery bypass grafting (CABG) due to significant luminal stenosis in unilateral or bilateral internal carotid arteries.[4] Neurological complications are the most dreaded complications for a cardiac surgeon. Addressing only carotid artery disease prior to CABG without any anticipatory preparation may cause perioperative myocardial ischemia, cardiac rhythm disturbances or rarely death. Present study is an attempt to compare synchronous intervention with staged surgical management in patients with concomitant carotid and coronary artery disease, considering early mortality and stroke as the important primary endpoints.

Materials and Methods

We obtained data from the Department of Medical Records, Sri Jayadeva Institute of Cardiovascular Sciences and Research, with accrual period from April 2013 to March 2017. In our unit, 432 patients underwent CABG during this study period, of which 42 patients had significant carotid artery disease. All patients underwent routine standard coronary angiography to assess coronary arteries. Pre-operatively, carotid duplex ultrasound scans were done in all patients and computer tomography-angiography of neck vessels when indicated.

Most of our patients had concomitant minimal carotid artery disease. Only those patients who had significant carotid artery disease and needed intervention were enrolled for the study.

Patients were assigned into two groups based on the severity of their coronary and carotid artery disease. Presence of unstable angina, left main coronary disease, left ventricular dysfunction and severely stenosed triple vessel disease would get them placed in the synchronous group. These 42 patients were then studied as follows. Group 1 constituted 20 patients who underwent simultaneous/synchronous procedures and group 2 comprised 22 patients who underwent staged procedures within 30 days apart.

Inclusion criteria

All patients with coronary artery disease undergoing CABG with concomitant carotid artery stenosis of 70% or more.

Exclusion criteria

Total occlusion of internal carotid artery, severe stenosis of the intracranial part of internal carotid artery and non-atherosclerotic carotid stenosis (dissection, tumour or mobile thrombus). Evidence of intracranial bleeding within the past 90 days. Significant valvular lesion requiring surgery, emergency CABGs, patients with post-MI VSR and left ventricular aneurysm.

Statistical analysis

The analysis was done in R statistical software (open source platform). Collected data was tested for normalcy before compilation. Multivariate logistic regression model was employed to test the hypothetical statements. Each variable's Probability value was extracted at fixed confidence interval CI-99%.

Study Endpoints

Mortality and stroke were the primary end points of our study. Secondary endpoints were postoperative bleeding, convulsions, transient ischemic attacks, reversible ischemic neurological deficits, recurrent laryngeal nerve paralysis and major adverse cardiac events like MI during the perioperative period. A stroke is characterised by a fixed, non-progressive neurologic deficit that lasts longer than 24 hours and is due to cerebral infarction. Reversible ischemic neurological deficit is defined as a lesion due to ischemia (and not infarction) presenting with weakness, paresis/paralysis or speech abnormalities lasting between 1–21 days followed by either a complete recovery

or residual deficits. Transient ischemic attacks recover within 24 hours and leave behind no neurological deficits.

Surgical Procedures

Coronary revascularization and carotid endarterectomy were done in all patients in synchronous or staged manner. All our patients had unilateral, significant carotid disease with or without mild disease on the contralateral side. There were no patients with total internal carotid occlusion. All procedures were performed by the same operative team. All synchronous procedures were performed under general anaesthesia administration. Head placement was done carefully to prevent compromise of the collateral blood supply. CEA team would proceed with exposing the carotid artery. Meanwhile, saphenous vein harvesting would commence.

After systemic heparinisation, carotid endarterectomy would be done. Intraoperative carotid shunts were used selectively based on the evaluation of collateral blood flow. Intraoperative blood pressure, cardiac rate and rhythm were continuously monitored and maintained especially during periods of arterial clamping. Following this, CABG was done off-pump in all our cases. Patients who underwent staged procedures, underwent carotid endarterectomy and then off pump CABG surgery within a period of 30 days on a different date. An integrated treatment approach involving the timing of carotid endarterectomy (CEA) for patients who have both carotid and coronary artery disease is favoured by many surgeons.[5] In this approach, patients with concomitant disease are treated in either a staged (CEA first, followed by coronary revascularization [CABG] at a second operation) or synchronous procedure (CEA and CABG during the same period of anaesthesia) based on the severity of the coronary stenosis.

This approach evolved in an attempt to minimize the adverse outcomes of stroke and death, which were found to be increased in early, influential studies examining the simultaneous treatment of concomitant disease.[6, 7]

Patient characteristics

Group 1 – Total 20 patients underwent synchronous procedures; CEA followed by CABG.

Group 2 – Total 22 patients underwent staged procedures, upto 30 days apart.

Results

Patients underwent CABG in our unit in Sri Jayadeva Institute of Cardiovascular Sciences and Research from April 2013 to March 2017; of which 42 patients had unilateral, significant carotid artery disease. The average age of the study population was 61 years. 24 of them were in the age groups between 55–65 yrs. Patients were assigned into two groups after explaining about the risks and benefits of both the surgical strategies. Patients with severe coronary artery stenosis, severe LMCA disease, unstable angina and with severe left ventricular dysfunction were preferentially added to the synchronous group. 20 patients underwent synchronous procedure – carotid endarterectomy followed by myocardial revascularisation under general anesthesia. The other group of 22 patients who underwent a staged procedure within 30 days apart had chronic stable angina with good LV function. The average age of the study population was 60 years, with a male preponderance in both the groups constituting about 80% of the study group. A significant percentage (40%) of the study population were smokers. Patients of both groups had other co-morbidities like hypertension, diabetes mellitus and dyslipidemia which possibly contributed to the accelerated progression of atherosclerosis. In synchronous group, 14 patients (70%) were hypertensive, 11 (55%) were diabetic and 9 (45%) were dyslipidemic. Similarly, in the staged group, 17 patients (77%) were hypertensive, 11(50%) were diabetic and 10 (45%) were dyslipidemic. 7 patients

Table 1 Patients characteristics measured by different attributes

Patient characteristics	Group 1	Group 2	P-value
Number of patients	20	22	—
Age (years) – average	61	59.7	≤ 0.001
Gender [Male/Female]	16/ 4	17/ 5	≥0.002
Smoking history	9 (45%)	8 (36%)	≤0.000
Hypertension	14 (70%)	17 (77%)	≤0.001
Diabetes Mellitus	11 (55%)	11 (50%)	≤0.000
Dyslipidemia	9 (45%)	10 (45%)	≥0.000
LMCA disease	7 (35%)	10 (45%)	≤0.000
Renal dysfunction	3 (15%)	4 (18%)	≤0.003

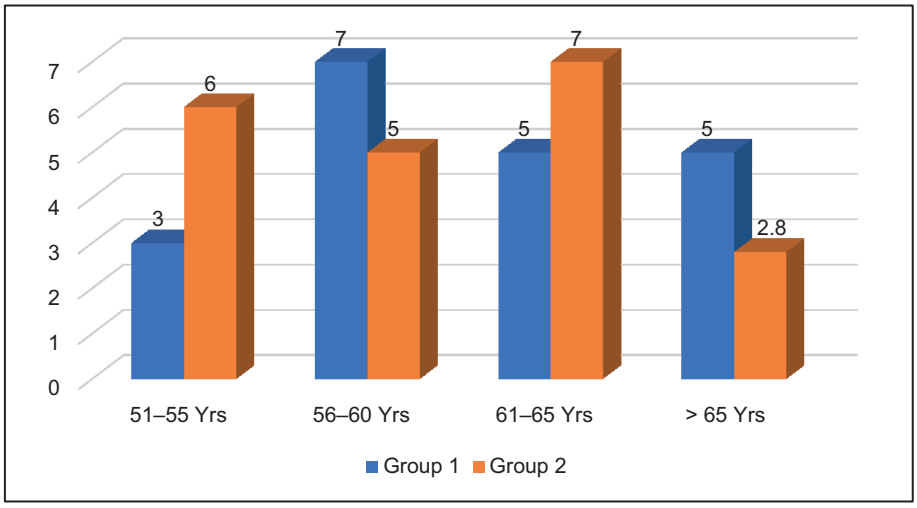

Figure 1 Age-wise distribution of Groups 1 and 2.

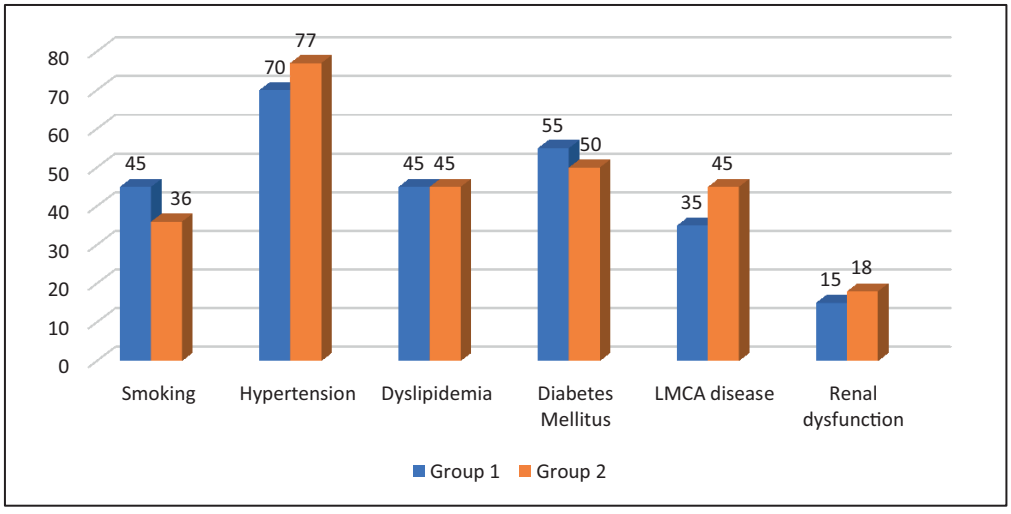

Figure 2 Patient characteristics in groups 1 and 2 (percentage of patients).

(35%) in synchronous group and 10 (45%) in staged group had a significant left main coronary disease. Renal dysfunction was seen in 3 patients (15%) in the synchronous group and 4 patients (18%) in the staged group.

Patients posted for CABG were on anti-platelet medications. These were stopped 5 days prior to synchronous procedure and intravenous heparin started if patients had critical coronary artery disease. In case of staged procedure, patients were started on dual anti-platelets soon after the CEA and then were operated within next few weeks. Dual antiplatelet drugs were again stopped 5 days prior and patients were put on intravenous heparin to prevent any in-hospital ischemic events. Post-operative bleeding requiring re-exploration was seen in only one patient (4.5%) in the staged group. Bleeding was from the chest wound. Two patients (10%) in the synchronous group and one patient (4.5%) [p>0.001] in the staged group had stroke on the ipsilateral side. Three patients (15%) from synchronous group had reversible ischemic neurological deficit. Two patients had paresis of the left upper limb and one had paresis of the right lower limb which gradually improved over next few weeks. Convulsions were seen in four patients (20%) from the synchronous group and one patient (4.5%) [p>0.001] from the staged group. Anti-convulsant

Table 2 Final out come of the study: correlation with Groups 1 and 2.

Endpoints of study	Group 1	Group 2	P-value
Re-exploration	0	1 (4.5%)	—
Stroke	2 (10%)	1 (4.5%)	≥0.001
Reversible Ischemic Neurological Deficit	3 (15%)	0	≥0.001
Convulsions	4 (20%)	1 (4.5%)	≥0.001
Myocardial Infarction	0	0	—
Death	0	0	—
Post operative hospital stay (days)	9.7 ± 2.5	15.4 ± 3.7	≤0.001

medications were started and continued in the post operative period. They were gradually tapered off in the next few months as per the neurologist's advice.

Cumulative adverse neurological events in the immediate post-operative period was found to be higher in the synchronous group. None of the patients had myocardial infarction or death during the perioperative period. Post operative hospital stay, as expected, was less in the synchronous group with an average of 9.7 days whereas in the staged group it was an average of 15.4 days. Patients have been regularly followed up in the out-patient department. At the end of one year and three years follow up period, there have been no major adverse cardiovascular or cerebral events in any of the patients.

Discussion

Coronary artery disease needs surgical intervention when the arteries have significant stenosis of >70%, have LMCA disease, multi-segment and multi-vessel involvement with critically stenosed vessels not amenable for percutaneous interventions and if there is left ventricular dysfunction.[8] Surgery can be done either on-pump or off pump if the distal targets are good in size and there is a viable myocardium to revascularize. Patients with poor left ventricular ejection fraction, critically stenosed multi-segment involved vessels with unstable hemodynamics will warrant an on-pump surgery since the heart may not tolerate dislocation well during distal anastomoses. Carotid artery disease needs intervention when the stenosis is greater than 70%. It may be symptomatic or asymptomatic. It may be unilateral, bilateral or may have near total or total occlusion on one side. Treatment options depend on the severity of the disease and include medical therapy alone with dual anti-platelets, anti-hypertensives and statins, carotid artery stenting or carotid endarterectomy.[8] The largest multicentre trial to-date – the Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST), International Carotid Stenting Study (ICSS) and Asymtomatic Carotid Trial-1 (ACT-1) in the recent times have all showed non-inferiority of stenting over endarterectomy.[9] Concomitant coronary and carotid artery disease can be addressed in many ways: synchronous carotid endarterectomy

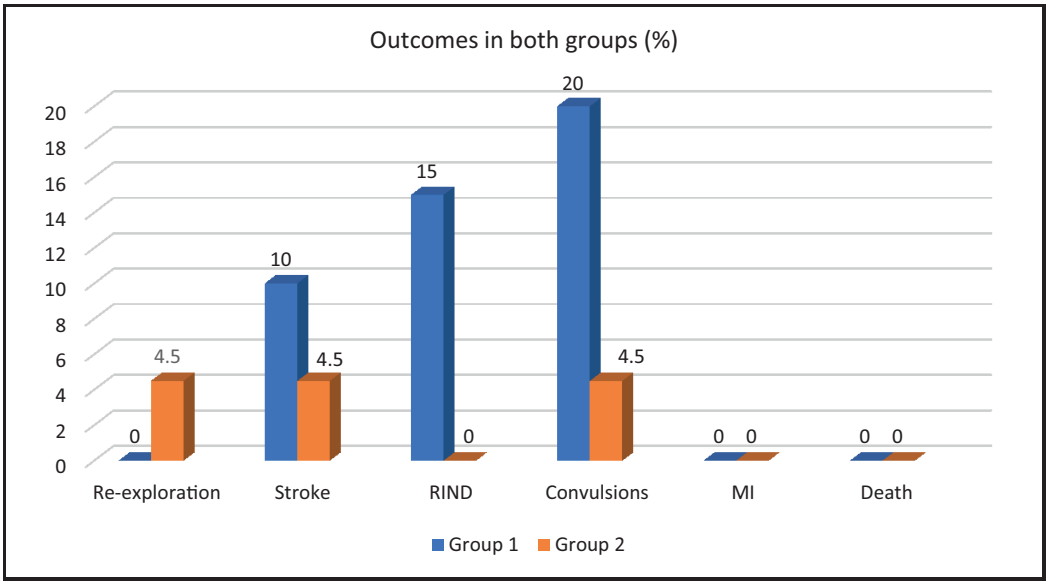

Figure 3 Surgical outcomes in both the groups.

with CABG, staged CEA followed by CABG within 30 days apart, synchronous or staged carotid artery stenting followed by CABG or reverse staged where CABG is performed first followed by carotid endarterectomy. Most authors are reluctant to do CEA on both sides for bilateral disease and prefer to address the more stenotic lesion first and address the contralateral side after performing CABG. The frequency of combined /synchronous CEA with CABG procedure ranges from 0.7- 4.2% among all patients who need myocardial revascularisation.[10] The timing of surgical procedures for concurrent carotid and coronary artery disease is among the most serious conundrums that cardiac, neuro and vascular surgeons have confronted during the past three decades.

Performing CABG in patients with severe carotid disease by maintaining adequate cerebral perfusion is a considerable challenge. The lower mean arterial pressures of cardiopulmonary bypass, systemic vasodilatory response and plaque embolism during aortic cannulation or cross-clamping increase the chances of perioperative stroke in CABG patients. Similarly, in patients who undergo off-pump procedures, the intermittent hypotension associated with positioning the heart could potentially impair cerebral perfusion. Vascular surgeons are concerned about the risk of perioperative myocardial infarction in patients with concurrent disease when intervention on the carotid artery is contemplated. Reverse staged procedures where CABG is followed by CEA has highest risk of ipsilateral stroke and lowest risk of MI. Hence most surgeons prefer synchronous or staged procedures to reverse staged procedure.

Synchronous procedure offers the benefit of single exposure to anesthesia, lesser duration of hospital stay and thus lesser expenditure to the patient. Khaitan et al, Shwartz et al and Minami et al have conducted studies independently using cardiopulmonary bypass while performing CABG after CEA in the synchronous procedure. They have shown results similar to using off pump CABG in terms of peri-operative rates of stroke, MI and mortality. They believed that extracorporeal circulation would offer neuroprotection due to hypothermia which would reduce oxygen requirement of brain and decrease the production of anoxic brain metabolites.

However, works of Borger et al and Coyle et al have shown higher morbidity and mortality after synchronous surgery rather than the staged procedure using off pump CABG. Studies of synchronous surgery by Fichino et al have shown perioperative rates of stroke at 5.6%, TIA at 6.6% and 8.6% mortality. A review of 16 papers on synchronous procedures of CEA followed by off-pump CABG by Rizzo et al reflected similar perioperative rates of stroke (5.6%), AMI(3%) and mortality (4.8%). Noteworthy is the benefit of off-pump CABG probably from avoiding the lower perfusion pressures associated with cardiopulmonary bypass. Further, the recent meta-analysis by Sharma et al in 2014, reviewing literature, encompassing 12 full text articles found that, between the synchronous and staged groups, there was not much of a difference in the two groups for perioperative rates of stroke, mortality of AMI. Similar results and opinion were expressed in a study by Mishra Y et al.[11] Refinement in surgical techniques and medical therapy may explain the difference between this study and the older ones reporting higher perioperative rates for these endpoints. Other single-center studies have also supported the economic benefits of synchronous CEA with CABG and the shorter hospital length of stay it requires.[12,13] The staged approach was associated with higher hospital charges and longer hospital stays.

In our study, in the synchronous group, perioperative rates of stroke was 10%, reversible ischemic neurological deficits was 15% and convulsions was 20%. This was much higher than that of the staged procedures we undertook in our comparative study which showed rates of 4.5% for stroke, 4.5% for convulsions and 0% for RIND. We had no incidence of acute MI, surgical site infections or mortality. Our study showed a post operative stay of an average 15 days for staged procedure versus 9 days for a synchronous procedure. However, it should be remembered that patients with severely stenosed carotid and coronary arteries, hypertension, poorly controlled diabetes, dyslipidemia, chronic smoking habits and critically stenosed triple vessel disease with left ventricular dysfunction were usually placed in the synchronous group. That may explain the high morbidity rates in the synchronous groups as was found in many studies.

Conclusion

The dilemma regarding the timing and type of surgical intervention (synchronous vs staged) is likely to continue. We feel that the synchronous versus

staged approaches should be titrated according to individual patient requirement with attention to associated co-morbidities. Patients with critically stenosed coronary and carotid artery lesions with accompanying severe co-morbidities should undergo synchronous procedures with CEA followed by CABG. Compared to the synchronous approach, the staged approach appears to have a lower overall complication rate but prolonged hospital stay. Staged approach may be better in patients with chronic stable angina and lesser co-morbidities.

Conflict of interest

None

Financial disclosures

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