International Journal of Cardiovascular and Thoracic Surgery
2021; 7(3): 20-29
http://www.sciencepublishinggroup.com/j/ijcts
doi: 10.11648/j.ijcts.20210702.13
ISSN: 2575-4866 (Print); ISSN: 2575-4882 (Online)

Prospective Analysis of Prevalence of Carotid Artery Disease and Neurological Outcomes After CABG in Patients with Significant Carotid Artery Disease

Shailesh Kumar Yadav

Cardiovascular Thoracic Surgery, Fortis Escorts Heart Institute, New Delhi, India

Email address:
shailurims@gmail.com

To cite this article:
Shailesh Kumar Yadav. Prospective Analysis of Prevalence of Carotid Artery Disease and Neurological Outcomes After CABG in Patients with Significant Carotid Artery Disease. *International Journal of Cardiovascular and Thoracic Surgery*. Vol. 7, No. 3, 2021, pp. 20-29.
doi: 10.11648/j.ijcts.20210702.13

Received: May 6, 2021; **Accepted**: May 21, 2021; **Published**: May 31, 2021

Abstract: CABG surgery is the utmost frequently performed major cardiovascular operation. Carotid artery stenosis is present-day in 6% to 8% of all patients undergoing CABG and is related with an increased risk of stroke during and after CABG. It is well recognized that the presence of carotid artery stenosis is a significant forecaster of poor consequences in patients undergoing coronary bypass graft surgery (CABG). The incidence of coexisting coronary and carotid artery disease varies between 2% and 14% and approximately 8% of patients undergoing CABG have a significant stenosis in an extra cranial carotid artery. The stated occurrence of carotid artery disease in patients experiencing cardiac surgery has diverse from 2 to 22%, with an average of 8% increasing with age. This prospective observational study was conducted in patients undergoing off-pump coronary artery bypass grafting with carotid artery stenosis from May 2015 to Feb 2017. A total of 2126 patients were observed and classified to three groups based on the grade of carotid artery stenosis in which 221 patients (group A) were Symptomatic or (asymptomatic with ≥ 70% carotid stenosis, unilateral or bilateral), 583 patients (group B) < 70% carotid stenosis, unilateral or bilateral and asymptomatic and 1332 patients (group C) No carotid stenosis. 221 patients were having ≥ 70% Carotid stenosis of which 95% of patients undertook CABG and 4.52% patients undertook CABG with carotid endartrectomy. 583 patients were having < 70% Carotid stenosis of which 99.7% patients undertook CABG. 1322 patients were without Carotid stenosis and all the patients underwent CABG. The nasty age of the patients in group A was 60.93±9.03, in group B 61.30±9.49 and in group C are 61.91±8.95, p=0.18. Postoperative TIA showed statistically noteworthy between the groups p=<0.0001. Means of hospital stay was more in patients with >70% carotid stenosis group (p=0.0004). In our study 6 patients (2.71%) presented with stroke in group A. The frequency in group B and C were 0.69% and 0.08% respectively, and were statistically (p=<0.001). Most of the patients in group A had experienced concomitment endarctectomy of carotid with (4.52%) compared to group B and C (0.17% and 0%). The occurrence of previous history of stroke/TIA was higher in group A compared to other groups (p<0.001) [Previous h/o stroke was seen in 74 (6.3%), 32 (5.4%) and 29 (2.19%) patients in respective groups]. Previous history of stroke has proved a vital role in decisive the outcome of these patients. Higher grade of Carotid stenosis doesn't affect mortality, ICU stay and the need for dialysis as proved in this study.

Keywords: Coronary Artery Bypass Grafting, Stroke, Carotid Stenosis

1. Introduction

Coronary artery bypass graft (CABG) surgery is the utmost frequently performed major cardiovascular operation. Carotid artery stenosis is present-day in 6% to 8% of all patients undergoing CABG and is related with an increased risk of stroke during and after CABG [1, 2]. It is well recognized that the presence of carotid artery stenosis is a significant forecaster of poor consequences in patients undergoing coronary bypass graft surgery (CABG) [3]. The occurrence of coexisting coronary and carotid artery disease varies between 2% and 14% and approximately 8% of patients undergoing CABG have a significant stenosis in an extra cranial carotid artery [4].

A number of studies have shown that the presence of carotid artery stenosis (CAS) in subjects undertaking cardiopulmonary bypass procedures increases the risk of significant neurological deficits [1, 5-10]. Intraoperative hemodynamic variability and anemia with subsequent cerebral hypo perfusion particularly in patients with extra cranial carotid disease may account for a significant number of intraoperative procedures. Additionally, studies have shown a direct link between degree of carotid artery stenosis and risk of ipsilateral stroke [11]. The characteristically poor postoperative course of patients who develop stroke after CABG underscores the need for timely gratitude and alteration of factors that predispose to stroke.

Prophylactic action of asymptomatic accompanying carotid artery stenosis is attained in dissimilar conducts, by carotid artery angioplasty and stenting (CAS) or carotid endarterectomy (CEA), either instantaneously with CABG, before CABG, or deferred after CABG (staged or reverse staged) [12]. Newly, carotid artery stenting (CAS) has been announced as a dissimilar revascularization modality for patients with symptomatic or asymptomatic high-degree stenosis in the extra cranial carotid arteries [13].

Carotid endarterectomy (CEA) in the attendance of uncorrected coronary disease has been related with very high operational death (20%) chiefly due to myocardial infarction [14, 15]. Correspondingly, coronary revascularization in the occurrence of severe carotid disease is related with increased jeopardy (14%) of perioperative stroke [16]. Originally, Bernhard et al. [14] projected joint coronary revascularization and carotid endarterectomy in patients who had severe coronary and carotid artery disease, in instruction to decrease the morbidity and mortality in these patients.

Present strategies state (Class IIa; Level of Evidence C) that carotid endarterectomy (CEA) is possibly suggested before CABG or associated to CABG in patients with symptomatic carotid stenosis or in asymptomatic patients with a unilateral or bilateral internal carotid stenosis of 80% [17]. Though, the best managing of these patients still remains debatable in scientific exercise.

Carotid artery stenosis (CAS) is current in 10%-20% of patients experiencing CABG and books for 30% of stroke related with CABG [18], while the stroke occasion rate for asymptomatic patients with important carotid artery stenosis varieties from 2%-5% [16, 19-22]. Its etiology is multifactorial, counting cerebral embolization from iatrogenic deployment of atherosclerotic plaques, air/fat embolism, peripheral vascular disease (PVD), hemodynamic variations, cerebral hyperthermia, aortic dissection, particular micro emboli, emboli because of aortic arch disease, aortic "crunch" happening with cross-clamping or cannulation, air and fat emboli [23-26] and systemic inflammatory reaction [27].

Stroke is a calamitous complication of coronary artery bypass grafting with an occurrence of 2% [1]. The massive mainstream of these strokes happens postoperatively inside the first 24 hours and is related with a mortality rate of 25%. While the etiology of postoperative stroke is multifactorial, hypo perfusion rising from a harshly stenotic carotid artery or embolization from an ulcerated plaque, calcific debris from a diseased valve, or outline of air during the procedure are important mechanisms [28-31]. Certainly, the jeopardy of stroke in patients with carotid disease afterward CABG has been projected at 1.8% in patients with stenosis _50%, 3.2% in patients with stenosis between 50% and 99%, and 10% in patients with contralateral obstruction [1].

Freshly, the Reduction of Atherothrombosis for Continued Health registry (REACH) has revealed that a considerable fraction of patients with chronic coronary artery disease have related carotid cerebrovascular, low extremity artery diseases, or both [32]. The stated occurrence of carotid artery disease in patients experiencing cardiac surgery has diverse from 2 to 22%, with an average of 8% increasing with age. Severe carotid artery stenosis existence three times higher in patients 60 years of age or older [11, 33, 34]. Scientific forecasters other than age for significant carotid artery stenosis in patients measured for coronary surgery comprise: diabetes, peripheral vascular disease (PVD), left main coronary artery stenosis ≥60%, carotid bruit, prior stroke or transient ischemic attack, prior vascular operation, smoking, and female sex [11, 33, 34].

The primary aim of our study was to assess the prevalence of carotid artery disease in patients undergoing elective CABG and also the cerebrovascular outcomes after surgery in patients who have significant carotid artery disease.

2. Material and Methods

2.1. Primary Objectives

To study the prevalence of carotid artery disease in patients undergoing elective coronary artery bypass grafting surgery & incidence of post-operative stroke and transient ischemic attack after CABG in patients with carotid artery disease.

2.2. Secondary Objectives

To study the ICU stay, hospital stay, ventilation time, respiratory and renal dysfunction in patients undergoing CABG with carotid artery stenosis.

2.3. Patient Selection and Randomization

This prospective observational study was conducted in patients undergoing off-pump coronary artery bypass grafting with carotid artery stenosis from May 2015 to Feb 2017. A total of 2126 patients were observed and categorized to three groups based on the degree of carotid artery stenosis in which 221 patients (group A) were Symptomatic or (asymptomatic with ≥ 70% carotid stenosis, unilateral or bilateral), 583 patients (group B) < 70% carotid stenosis, unilateral or bilateral and asymptomatic and 1332 patients (group C) No carotid stenosis.

Informed consent was obtained from all patients who met the inclusion criteria

As this study aims at estimating the prevalence of carotid artery disease among patients undergoing CABG without any other cardiac procedure through a prospective study, the carotid stenosis for study is classified as the following:

-No carotid stenosis (C)
-Less than 70% stenosis, Unilateral or Bilateral (B)
-Greater than 70% stenosis Unilateral or Bilateral (A)

And further the three classes have been clubbed for analysis as two groups with No stenosis (C) as control group and the other two classes (A & B) as the cases group.

For the present prospective study, the number of cases considered with elective CABG during the study period is 794 and controls are 1321 and in all patients numbering 2115 have been studied. These increases in the actual sample sizes would improve the power of the test beyond 90% at same significance level of 95% and an increase of incidence of stroke on an average by 5% with varied degrees of carotid stenosis.

2.4. Inclusion Criteria

Patients with coronary artery disease planned for elective coronary artery bypass grafting.

Patients giving informed written consent.

2.5. Exclusion Criteria

Coronary artery bypass grafting with other cardiac procedure simultaneously.

Patients not giving consent.

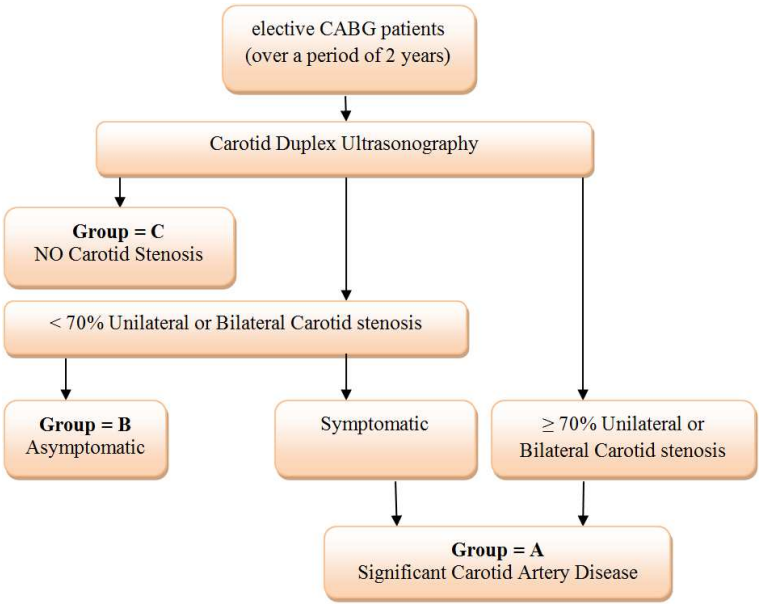

Figure 1. *Patient's selection.*

2.6. Duration of Study and Follow up

The duration of study period was for 2 years from May 2015 to Feb 2017 Participants were followed up during their index hospital admission and assessed at hospital discharge

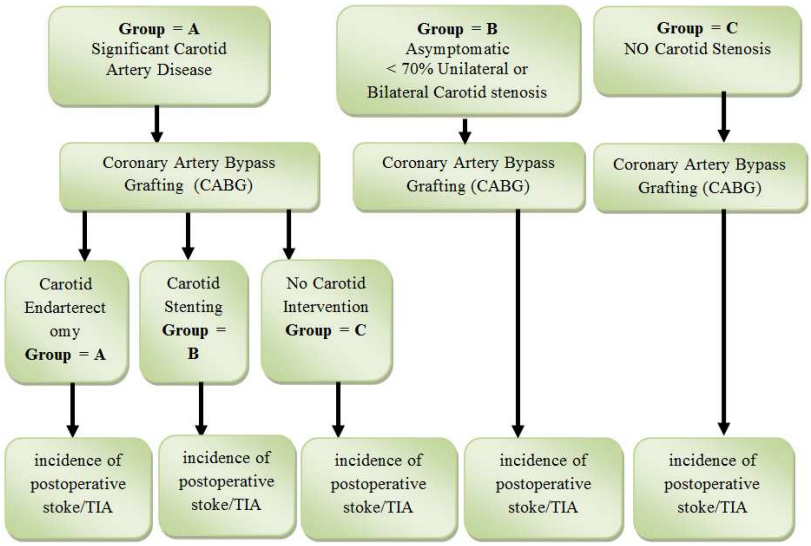

Figure 2. *Stroke rate in different patient groups.*

2.7. Statistical Analysis

Statistical scrutiny was did with SAS 9.2 version software. Incessant variables are articulated as mean ± standard deviation. Definite variables are articulated as raw numbers and percentages. The variances were scrutinized with a Chi-square or Fischer exact test and two sample T test. Logistic regression was applied on quantifiable totals to see their effect on the response variables. The Statistical implication for all the tests was acknowledged at a probability level <0.05.

3. Results

The nasty age of the patients in group A was 60.93±9.03, in group B 61.30±9.49 and in group C are 61.91±8.95, p=0.18 (table 1). The mean age of the patients in group C was slightly more compared to group A and B, the difference did not reach statistically significance (figure 1) More number of males (86.9%) presented with >70% carotid stenosis compared to females (13.12%). However there was observed no statistical difference between the groups (p=0.75) (figure 1)

Statistically no significant difference was observed between the baselines variables (table 1) which includes diabetes (p=0.16), hypertension (p=0.46), hyperlipidemia (p=0.66), previous MI (p=0.66), recent MI (p=0.92), atrial fibrillation (p=0.75), renal dysfunction (p=0.57) and CNS abnormalities (p=0.83).

Family history of carotid stenosis was observed in 30.77% patients in group A, 32.08% patients in group B and 31.69% patients in group C (p=0.93). Preoperative stenosis showed significant difference between the groups (6.3% of patients had preoperative stenosis in >70% carotid stenosis group, 5.42% of patients had preoperative stenosis in >70% carotid stenosis group, 2.19% of patients had preoperative stenosis in no carotid stenosis group, p=<0.0001) (table 1).

Table 1. *Baseline characteristics between the groups.*

Variables		≥ 70% Carotid stenosis (Group A=221)		< 70% Carotid stenosis (Group B=583)		No Carotid stenosis (Group C=1322)		P value
		No	%	No	%	No	%	
Age	Mean ±SD	60.93±9.03		61.30±9.49		61.91±8.95		0.18
Sex	Female	29	13.12	73	12.52	154	11.65	0.75
	Male	192	86.88	510	87.48	1168	88.35	
Diabetes	Yes	108	48.87	288	49.40	707	53.48	0.16
	No	113	51.13	295	50.60	615	46.52	
Hypertension	Yes	124	56.11	321	55.06	696	52.65	0.46
	No	97	43.89	262	44.94	626	47.35	
Hyperlipidaemia	Yes	123	55.66	305	52.35	695	52.57	0.66
	No	98	44.34	278	47.68	627	47.43	
NYHA	I	149	67.42	399	68.44	854	64.60	0.19
	II	37	16.74	102	17.50	275	20.80	
	III	32	14.48	68	11.66	176	13.31	
	IV	3	1.36	14	2.40	17	1.29	
EF	Mean ± SD	47.08±11.16		47.27±11.12		47.46±11.58		0.87
Previous MI	Yes	123	55.66	305	52.32	695	52.75	0.66
	No	98	44.34	278	47.68	627	47.43	
Recent MI	Yes	34	15.38	91	15.61	214	16.19	0.92
	No	187	84.62	492	84.39	1108	83.81	
Pre Card surgery	Yes	2	0.90	8	1.37	35	2.65	0.08
	No	219	99.10	575	98.63	1287	97.35	
AF	Yes	6	2.17	13	2.23	26	1.97	0.75
	No	215	97.29	570	97.77	1296	98.03	
Family History	Yes	68	30.77	187	32.08	419	31.69	0.93
	No	153	69.23	396	67.92	903	68.31	
Renal Dysfunction	Yes	38	17.19	98	16.81	201	15.20	0.57
	No	183	82.81	485	83.19	1121	84.80	
CNS	Yes	221	100.00	582	99.83	1320	99.85	0.83
	No	0	0.00	1	0.17	2	0.15	
Pre TIA Stroke	Yes	14	6.33	32	5.42	29	2.19	<.0001
	No	207	93.67	551	94.51	1293	97.81	

NYHA: New York Heart Association; EF: Ejection Fraction; MI: Myocardial Infraction; AF: Atrial Fibrillation; CNS: Central Nervous System; TIA: Transient Ischemic Attack.

Of 2126 patients, 221 patients were having ≥ 70% Carotid stenosis of which 95% of patients underwent CABG and 4.52% patients underwent CABG with carotid. 583 patients were having < 70% Carotid stenosis of which 99.7% patients underwent CABG. 1322 patients were without Carotid stenosis and all the patients underwent CABG (table 2).

Postoperative outcomes like mortality (p=0.93) respiratory complications (p=0.22), dialysis (p=0.43) were comparable between the groups. Postoperative TIA showed statistically significant between the groups (6 (2.71%) patients in group A

vs 4 (0.69%) patients in group B and 1 (0.008) patient in group C, p=<0.0001. Means of hospital stay was more in patients with >70% carotid stenosis group (p=0.0004). Ventilation time (p=0.93) and ICU stay (0.58) showed no difference between the three groups (table 3)

Age, previous cardiac surgery and previous stroke / TIA are acting as predictors of stroke for postoperative stroke/TIA. Patients in NYHA class III shows a trend towards developing postoperative stroke (table 4)

Table 2. *Results of Carotid Duplex scan.*

Variables	≥ 70% Carotid stenosis (Group A=221)		< 70% Carotid stenosis (Group B=583)		No Carotid stenosis (Group C=1322)	
	No	%	No	%	No	%
CABG	210	95.02	581	99.66	1322	100.00
CABG (mid cab)	0	0.00	1	0.17	0	0.00
CABG + Carotid	10	4.52	1	0.17	0	0.00
CABG + Carotid (mid cab)	1	0.45	0	0.00	0	0.00

CABG: Coronary Artery Bypass Graft

Table 3. *Postoperative outcomes between the groups.*

Variables		≥ 70% Carotid stenosis (Group A=221)		< 70% Carotid stenosis (Group B=583)		No Carotid stenosis (Group C=1322)		P value
		No	%	No	%	No	%	
Postoperative TIA Stroke	Yes	6	2.71	4	0.69	1	0.08	<.0001
	No	215	97.29	579	99.31	1321	99.92	
Ventilation time	Mean ± SD	1.09±0.30		1.10±0.31		1.10±0.30		0.93
Respiratory	Yes	11	4.98	17	2.92	59	4.46	0.22
	No	210	95.02	566	97.08	1263	95.54	
Dialysis	Yes	2	0.90	8	1.37	10	0.76	0.43
	No	219	99.10	575	98.63	1312	99.24	
ICU stay	Mean ± SD	2.32±0.76		2.26±0.67		2.28±0.69		0.58
Hospital stay	Mean ± SD	7.03±1.48		6.82±0.7		6.80±0.63		0.0004
Expired	Yes	4	1.81	12	2.06	24	1.84	0.93
	No	217	98.19	571	97.94	1298	98.18	

TIA: Transient Ischemic Attack; ICU: Intensive Care Unit

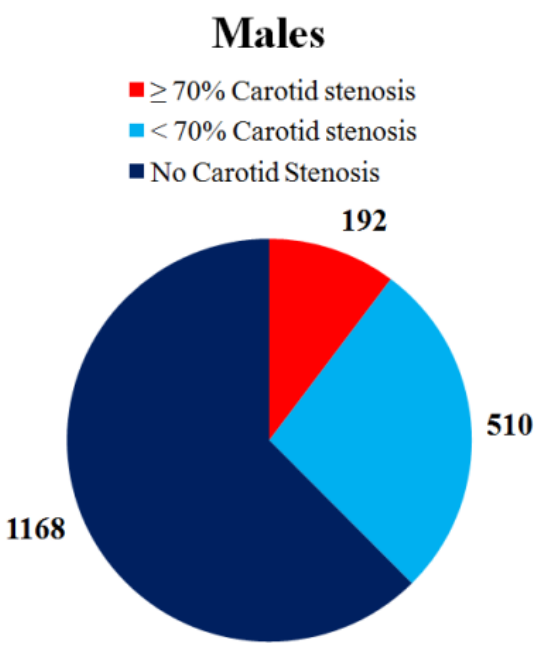

Figure 3. *Gender distribution between the group of males.*

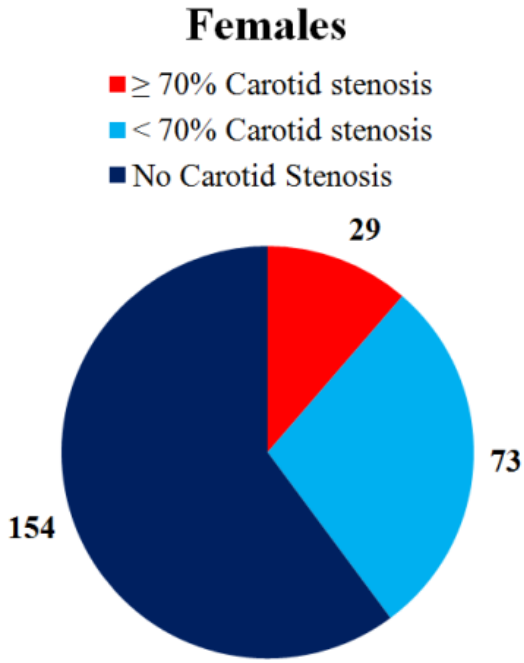

Figure 4. *Gender distribution between the group of females.*

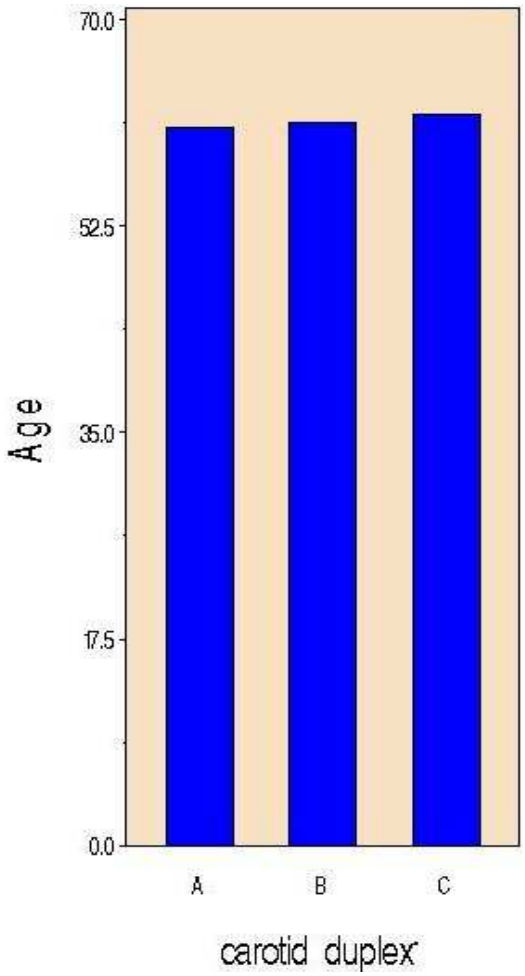

Figure 5. *Means of age of patients between the groups.*

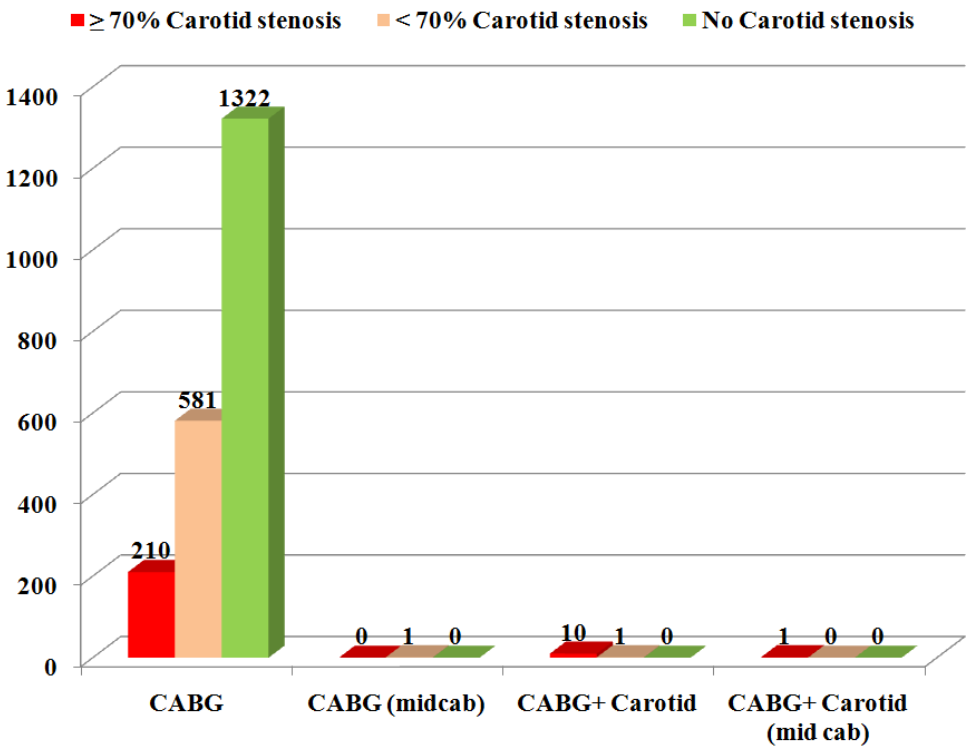

Figure 6. *Type of procedure performed between the groups.*

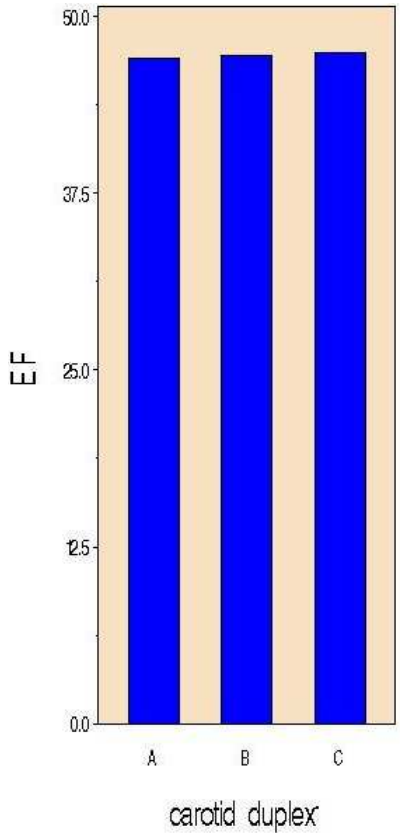

Figure 7. *Means of ejection fraction between the groups.*

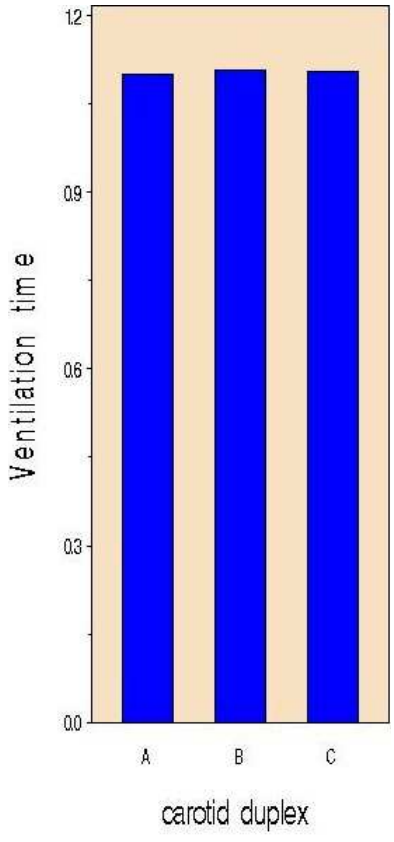

Figure 8. *Means of ventilation between the groups.*

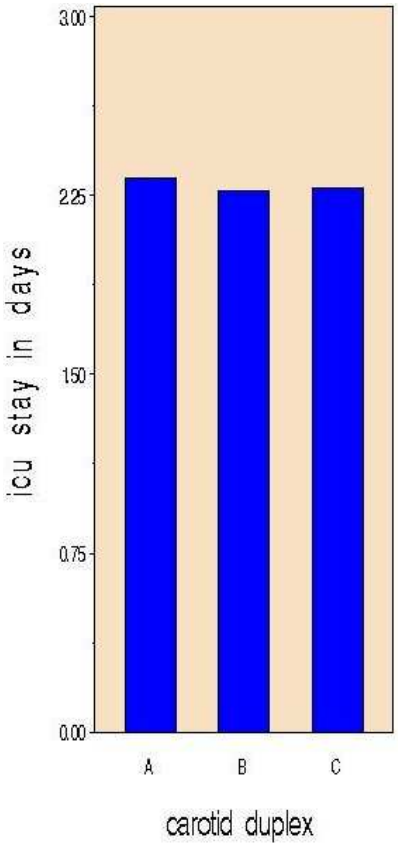

Figure 9. *Means of ICU between the groups.*

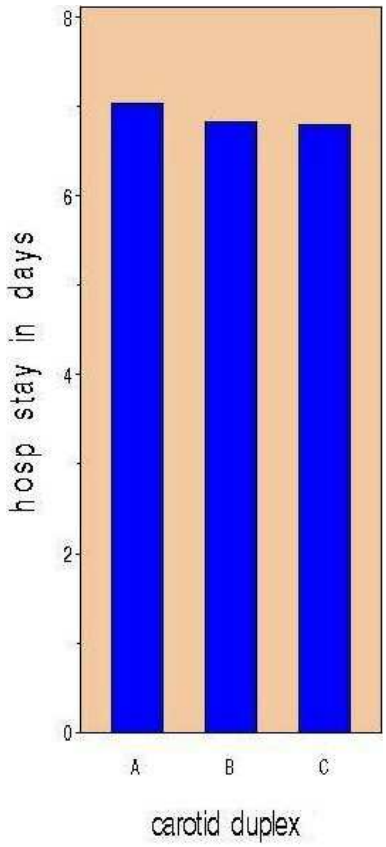

Figure 10. *Means of hospital stay between the groups.*

Table 4. *Predictors of postoperative stroke.*

Variable	P value
Age	0.02
Sex	0.29
DM	0.95
HTN	0.18
Hyperlipidaemia	0.99
NYHA	0.08
Previous cardiac surgery	0.05
AF	0.49
Family history	0.78
Renal dysfunction	0.23
CNS	0.96
Previous stroke/TIA	0.0001

DM: Diabetes Mellitus; HTN: Hypertension; NYHA: NewYork Heart Association; AF: Atrial Fibrillation; CNS: Central Nervous System; TIA: Transient Ischemic Attack.

4. Discussion

Incidence of CAS: Previous studies have revealed noteworthy CAS (Carotid Artery Stenosis) in patients undertaking CABG [35]. Prevalence of CAS increases with age. Pujia et al [36] stated that the occurrence of CAS of >50% was 5% in subjects ≥ 75 year of age. In Framingham study [37] 8% of 1189 members were registered and had carotid stenosis of >50%.

In our study mean age of the patients in all the three groups were 60.9±9 and were statistically insignificant. Number of males (86.9%) presented with >70%. CAS when compared to females, patients with >70% CAS accounted for 6.3% compared to 5.42 and 2.19% in group II and III which was statistically significant. This is reliable with preceding studies which have stated an occurrence of 6.1 – 31.7% in CABG patients [9, 10, 35, 38].

A connotation between Carotid Atherosclerosis and Coronary Artery Disease (CAD) has been previously recognized (Japanese study). Hence with increasing age, the incidence of Atherosclerosis of Carotid Artery increases amounting to higher prevalence of CAS particularly in male population.

Prevalence of stroke in patients with CAS undergoing CABG: Previous history of stroke was seen in 74 (6.3%), 32 (5.4%) and 29 (2.19%) patients between the groups. Post-operative TIA was seen in 6 (2.17%), 4 (6.9%) and 1 (0.08%) patients between the groups.

Incidence of stroke / TIA: Stroke is considered as one of the most overwhelming difficulty after CABG. The incidence reported is 2% [1]. Risk factors like old age, CAS, peripheral artery disease etc conditions play pivotal role in stroke after CABG.

In our study 6 patients (2.71%) presented with stroke in group A. The prevalence in group B and C were 0.69% and 0.08% respectively, and were statistically significant (p=<0.001) Most of the patients in group A had undergone concomitant endarctectomy of carotid with (4.52%) compared to group B and C (0.17% and 0%).

The risk of stroke increases with cumulative stenosis in Carotid Artery. One of the studies exposed that the risk of stroke was 1.8% with stenosis <50% and it rose to 3.2%with stenosis >50% and 10% with contralateral carotid occlusion [1]. A clear benefit with carotid endarctectomy has been proposed in these patients [39-41]. Patients with severe asymptomatic CAS, peripheral arterial disease conditions play pivotal role in occurrence of stroke after CABG.

The occurrence of stroke in this study is significantly higher in those with >70% Carotid artery disease. CAD may not be the stroke operating factor determining the outcome (stroke). Several other factors like Age, Male gender, Diabetes, Hypertension, previous MI and previous history of stroke may concurrently be responsible for the fatal outcome. Our study didn't demonstration significant statistical difference between the groups in terms of diabetes, HTN, Hyperlipidemia, Previous history of stroke etc.

However the presence of previous history of stroke/TIA was higher in group A compared to other groups (p<0.001) [Previous history of stroke was seen in 74 (6.3%), 32 (5.4%) and 29 (2.19%) patients in respective groups]. Previous history of stroke has proved to play a vital role in determining the outcome of these patients. Myocardial stunning after off-pump CABG is thought to be a critical factor in the development of postoperative stroke after CABG [42]. Asymptomatic patients with severe CAS may not present with post-operative stroke, in the absence of other risk factors mentioned earlier.

The low risk of stroke in this subset of patients has been confirmed by other studies as well [18, 43]. Evidence against a direct casual relation between post cardiac surgery stroke and significant CAS has been delineated by Li et al [43].

Prolonged hospital stay was observed in group A patients as compared with other groups (p=0.004). Higher grade of Carotid stenosis doesn't influence mortality, ICU stay and the need for dialysis as proved in this study. Mortality is the most feared complication post-operatively but is not modified by degree of stenosis in carotid alone, but requires other predisposing factors yet to be proved.

We had gone a step ahead to determine the prediction of stroke. Logistic regression analysis revealed that advancing age with previous history of stroke and or TIA are the strongest predictors of stroke in all the three groups. Other predisposing like DM, HTN, Hyperlipidemia, presence of Arrhythmias seen to play minimal or no role in the development of stroke. Causes of stroke may be multifactorial and interlinked. However the causes are subject to intense debate in the international literature. After CEA the causes of stroke may vary from embolization of thrombus from endartrectomy site to intracranial hemorrhage or hyper fusion syndrome [44]. Majority of post CABG strokes are encountered within 7 days postoperatively. Our study proves that CABG patients presenting with history of stroke were significantly more likely to suffer a further stroke if they were symptomatic.

5. Conclusion

The incidence of CAS determined by our study is at par

with National and international studies. Multiple risk factors were evaluated and the close link between them was proved to be vital in determining the prevalence of stroke in this cohort. Advancing age along with previous history of stroke and or TIA are proved to be the strongest predictions of stroke. An optimal therapeutic strategy is yet to be devised for prevention of stroke and other related complications for asymptomatic and symptomatic patients with CAS experiencing CABG.

6. Recommendations

1. The presence of severe carotid stenosis and carotid artery occlusion increases the incidence of perioperative stroke but may not affect the death rate among patients undergoing coronary artery bypass surgery.
2. The knowledge of the risk factors offers an opportunity to implement preoperative and intraoperative measures as well as to reduce the occurrence of stroke, and it should influence the patient selection.
3. Preoperative carotid scan is a mandatory prerequisite in all high risk individuals.

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