Early Outcome of Combined Carotid Artery Stenting with Coronary Artery Bypass Grafting

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Introduction. The efficient and optimal therapeutic management of patients with concomitant carotid and coronary artery disease requiring cardiac surgery is still presenting a significant clinical challenge. The avoidance of devastating complications as stroke, myocardial infarction, and death particularly within 30 days is important.

The aim of this work to evaluate the results of same-day revascularization of carotid artery disease by stenting (CAS) and coronary artery disease by coronary artery bypass grafting (CABG).

Subject and methods. A total of thirty consecutive patients with concurrent severe carotid and coronary artery disease underwent same-day synchronous CAS and urgent CABG between January 2012 and January 2015 were included in the study. All procedures were performed at a single centre in Cairo university hospital. The study cohort was characterized according to demographic and clinical characteristics, which included degree of carotid stenosis, presence/absence of preoperative neurological symptoms, and cardiac operative risk profile. All patients underwent CAS under embolic protection devices and then CABG was done on the same day. Tirofiban infusion was started one hour before stinting procedure and was maintained for 4 hours after, then discontinued 2 hours before surgery. The primary end point of the study was the composite incidence rate of myocardial infarction, stroke, and death 30 days after CAS-CABG. All patients underwent on pump CABG, and dual Clopidogrel and aspirin antiplatelet regimen was initiated once postoperative bleeding was not suspected.

Results. There were 23 males and 7 females enrolled in our study, the mean age was 66.93 years. 17 patients were diabetics (56.7%), and 13 patients were hypertensive (43.3%). All patients had good LV function prior to surgery. Peripheral vascular disease was present in 6 patients (20.0%). As for the coronary affection, 5 patients had left main disease (16.7%), 14 patients had triple vessel disease (46.7%), and 14 patients had proximal LAD disease (46.7%). One patient had concomitant aortic valve replacement with CABG. Patients who had RICA stenting (20 patients) had a mean stenosis of 80% on this side with a mean of 38% in the contra lateral side. Patients who had LICA stenting (10 patients) had a mean stenosis of 83% on this side together with a mean of 37% in the contra lateral side (statistically insignificant). There was no major or minor strokes or MI during the follow up period. A single patient had drop of blood pressure following carotid stinting prior to surgery however, this patient had CABG surgery after stabilization of the blood pressure with no complications postoperatively. Whereas only one patient had postoperative bleeding following CABG. The non-survived patient who had a RICA stent prior to a concomitant surgery for aortic valve replacement and CABG died during the followup period, 2 days postoperatively due to intractable arrhythmias.

Conclusion. Same-day approach appeared safe in terms of early -term results, this appeared not only for low; in-hospital mortality, but also for CAS procedures and the rate of stroke and myocardial infarction which seemed extremely lower than was expected. Long-term survival needed to be studied to confirm these satisfactory results, thus confirming the valid therapeutic approach option for all patients with significant internal carotid artery stenosis associated with coronary and other cardiac lesions. Thus planned carotid stenting followed by CABG is a viable method of treatment for patients with coexistent carotid and coronary atherosclerosis.

Key Wards: carotid stenting procedure - CABG - stroke- myocardial infarction

Introduction.

Carotid endarterectomy (CEA) has been shown to reduce the incidence of stroke in patients with symptomatic and asymptomatic carotid stenosis [1,2]. With ongoing advances in endovascular technology and increasing experience with CAS on the part of interventionists [3, 4]. Recently, carotid artery stenting (CAS) has been introduced as an alternative revascularization modality for patients with symptomatic or asymptomatic high-degree stenosis in the extracranial carotid arteries [5]. Several randomized studies and registries have shown similar outcomes when compared with CEA in high-risk populations [6,7]. This approach has been postulated and recently used by several groups as a less risky alternative to CEA in patients with indication for CABG. As carotid artery stenosis is often associated with advanced coronary artery disease. The coexistence of carotid and coronary artery disease adds complexity to the medical decision process and brings increasing challenge to the perioperative management of coronary artery bypass graft (CABG) surgery [8]. Carotid artery stenting (CAS) is a minimally invasive technique for treating carotid artery disease. However, limited information is available in the literature to support this indication. 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 extracranial carotid artery[8]. Also, the update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment, carotid artery stenting (CAS) is indicated as an alternative to carotid endarterectomy (CEA) for the management of symptomatic carotid patients[9]. According to these recommendations, CAS is preferred to CEA in symptomatic patients with specific technical, anatomic, or physiological characteristics that render these individuals at "high risk" for surgery (e.g., contralateral carotid occlusion, previous neck irradiation, recurrent carotid stenosis, and so forth)[10]. Actually prioritization based on the symptomatic vascular territory, local expertise with an integrated team approach by interventionists, neurologists and cardiothoracic surgeons, preferably in high-volume centers .The current study represents a trial to get information regarding outcomes in patients undergoing staged CAS followed by CABG.

Subject and methods.

In a prospective, nonrandomized study, we analyzed 30 consecutive patients that underwent CAS followed by cardiac surgery from January 2012 to January 2015 at our center. The study protocol was approved by the Ethics Committee of our hospital and all patients gave written informed consent.

The indications for cardiac surgery were established before the carotid angioplasty. At Cairo university hospital, all patients scheduled for cardiac surgery are screened preoperatively by color duplex ultrasonography for carotid disease. The estimation of the degree of carotid stenosis is based on Nicolaides criteria [11]. Our policy is to treat symptomatic patients with >60% carotid stenosis and asymptomatic patients with \geq 80% stenosis. If both carotid arteries are involved, we treat the symptomatic side or the side with the more severe stenosis in asymptomatic patients. All patients with concurrent severe carotid and coronary artery disease underwent same-day synchronous CAS and urgent CABG between were prepared for the procdures. All procedures were performed at a single centre in Cairo university hospital. On admission to ICU full medical history from the patient (if possible) or his/ her relatives, full clinical examination, plain chest X-ray and ECHO heart. Arterial blood gas analysis, Serum electrolytes (Na, K, Cl, Mg, Ca), renal function, hematocrit ,serum albumin,SGPT,SGOT and coagulation profile were carried out for all patients. Full neurological assessment of all patients before the procedure was done carefully. The study cohort was characterized according to demographic and clinical characteristics, which included degree of carotid stenosis, presence/absence of preoperative neurological symptoms, and cardiac operative risk profile. All patients underwent CAS under embolic protection devices and then CABG was done on the same day. Tirofiban infusion was started one hour before stenting procedure and was maintained for 4 hours after, then discontinued 2 hours before surgery. The dosage of tirofiban includes a 30 min loading dose of 0.4 µg kg-1 min-1 followed by an infusion of 0.1–0.15 µg kg-1 min-1. Tirofiban has a plasma half-life of 1.5–2 h. It is removed by both renal and biliary excretion. Patients with renal insufficiency require dose adjustment of tirofiban .The primary end point of the study was the composite incidence rate of myocardial infarction, stroke, and death 30 days after CAS-CABG. All patients underwent on pump CABG, and dual Clopidogrel and asprin antiplatelet regimen was initiated once postoperative bleeding was not suspected. Quantitative variables are presented as mean \pm SD and qualitative data are given as number and percentage. Normal distribution of data was tested via Kolmogorov-Smirnov test and by Fisher's exact test for categorical variables. All tests were two-sided, and p < 0.05indicated a statistical significance.

Results.

There were 23 males (76.7%) and 7 females (23.3%). The mean age was 66.93 years. 17 patients were diabetics (56.7%), and 13 patients were hypertensive (43.3%). Peripheral vascular disease was present in 6 patients (20.0%). As for the coronary affection, 5 patients had left main disease (16.7%), 14 patients had triple vessel disease (46.7%), and 14 patients had proximal LAD disease (46.7%). One patient had concomitant aortic valve replacement with CABG.

Table (1)	demographic data
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S	ide	
Right	Left	Total

Sex	Male	Count	17	6	23
		% within Side	85.0%	60.0%	76.7%
	Female	Count	3	4	7
		% within Side	15.0%	40.0%	23.3%
Tota	I	Count	20	10	30
		% within Side	100.0%	100.0%	100.0%

Table(2) diabetic patients

			Si	de	
			Right	Left	Total
Diabetic	Yes	Count	11	6	17
		% within Side	55.0%	60.0%	56.7%
	No	Count	9	4	13
		% within Side	45.0%	40.0%	43.3%
Total		Count	20	10	30
		% within Side	100.0%	100.0%	100.0%

hypertensive patients Table(3)

			Sie	de	
			Right	Left	Total
hyperte	Yes	Count	٨	0	١٣
nsive		% within Side	40 %	۰۰%	٤٣,٣%
	No	Count	۲۱	٥	11
		% within Side	٦٠%	۰۰%	٥٦,٧%
Total		Count	۲.	۱.	۳.
		% within Side	۱۰۰%	۱۰۰%	۱۰۰%

	-		Si	de	
			Right	Left	Total
PVD	Yes	Count	3	3	6
		% within Side	15.0%	30.0%	20.0%
	No	Count	17	7	24
		% within Side	85.0%	70.0%	80.0%
Total	-	Count	20	10	30
		% within Side	100.0%	100.0%	100.0%

Table (4) peripheral vascular disease

	-		Si	de	
			Right	Left	Total
LMD	Yes	Count	3	2	5
		% within Side	15.0%	20.0%	16.7%
	No	Count	17	8	25
		% within Side	85.0%	80.0%	83.3%

Total	Count	20	10	30
	% within Side	100.0%	100.0%	100.0%

Table (0) triple vessel disease						
			Sic	de		
			Right	Left	Total	
Triple Vessel	Yes	Count	10	4	14	
		% within Side	50.0%	40.0%	46.7%	
	No	Count	10	6	16	
		% within Side	50.0%	60.0%	53.3%	
Total		Count	20	10	30	
		% within Side	100.0%	100.0%	100.0%	

Table (C) triple vessel disease

Table(7) proximal LAD

	-		Si		
			Right	Left	Total
Proximal	Yes	Count	8	6	14
Stenosis LAD		% within Side	40.0%	60.0%	46.7%
	No	Count	12	4	16
		% within Side	60.0%	40.0%	53.3%
Total	-	Count	20	10	30
		% within Side	100.0%	100.0%	100.0%

The mean ejection fraction for patients who had right internal carotid artery (RICA) stenting was 51.55%, while for those with left internal carotid artery (LICA) stenting the mean ejection fraction was 53.00% (statistically insignificant). The mean ejection fraction for all patients was 52,03% which indicates that all patients had good LV function prior to surgery. Patients who had RICA stenting (20 patients) had a mean stenosis of 80% on this side with a mean of 38% in the contralateral side. Patients who had LICA stenting (10 patients) had a mean stenosis of 83% on this side together with a mean of 37% in the contralateral side (statistically insignificant).

Table (8) lesions sides

Left_ICCA	Right_ICCA	Ejection_Fraction	Serum_Creat#	LDL	Age	Side	
0.38	0.80	51.55	1.18	195.15	66.65	Mean	Right
0.29	0.08	5.59	0.15	24.19	3.83	Std. Deviation	
.00	.60	44.00	1.00	150.00	60.00	Minimum	
1.00	.95	60.00	1.50	250.00	74.00	Maximum	
20	20	20	20	20	20	N	
0.83	0.37	53.00	1.34	194.40	67.50	Mean	Left
0.04	0.16	6.99	0.24	15.56	2.51	Std. Deviation	
.75	.15	38.00	1.10	173.00	63.00	Minimum	
.90	.60	60.00	1.90	220.00	72.00	Maximum	
10	10	10	10	10	10	N	
0.53	0.66	52.03	1.23	194.90	66.93	Mean	Total
0.32	0.24	6.01	0.20	21.42	3.42	Std. Deviation	_
.00	.15	38.00	1.00	150.00	60.00	Minimum	
1.00	.95	60.00	1.90	250.00	74.00	Maximum	
30	30	30	30	30	30	N	

The follow-up period of our study was the 1st 30 days following CABG surgery. 29 patients completed the follow-up period. One patients, who had a RICA stent prior to a concomitant surgery for aortic valve replacement and CABG, died during the follow-up period, 2 days postoperatively due to intractable arrythmias. This patient was also reopened at the same day of surgery as there was high possibility of bleeding for which surgical source was found. One patient suffered some drop of blood pressure following stenting of RICA, prior to surgery. However, this patient had CABG surgery after stabilization of the blood pressure with no complications postoperatively. There was no incidence of major or minor strokes during the follow-up period, and none of our patients had postoperative myocardial infarction. All patients in the study were discharged home at a mean of 6 days postoperatively.

			Stroke_Major	
			No	Total
Side	Right	Count	20	20
		% within Stroke_Major	66.7%	66.7%
	Left	Count	10	10
		% within Stroke_Major	33.3%	33.3%
Total	-	Count	30	30

Table (9) Major stroke

	-		Stroke_Major	
			No	Total
Side	Right	Count	20	20
		% within Stroke_Major	66.7%	66.7%
	Left	Count	10	10
		% within Stroke_Major	33.3%	33.3%
Total		Count	30	30
		% within Stroke_Major	100.0%	100.0%

Table (9) Major stroke

Table (10) Minor stroke

	-		Stroke_Minor	
			No	Total
Side	Right	Count	20	20
		% within Stroke_Minor	66.7%	66.7%
	Left	Count	10	10
		% within Stroke_Minor	33.3%	33.3%
Total	-	Count	30	30
		% within Stroke_Minor	100.0%	100.0%

$Table \ (11) \ \text{Postoperative myocardial infarction}$

			МІ	
			No	Total
Side	Right	Count	20	20
		% within MI	66.7%	66.7%
	Left	Count	10	10
		% within MI	33.3%	33.3%
Total	-	Count	30	30
		% within MI	100.0%	100.0%

Table (12)Blood pressure drop post stenting

Dec#_BP_	Post_PTA	
Yes	No	Total

Side	Right	Count	1	19	20
		% within Dec#_BP_Post_PTA	100.0%	65.5%	66.7%
	Left	Count	0	10	10
		% within Dec#_BP_Post_PTA	.0%	34.5%	33.3%
Total		Count	1	29	30
		% within Dec#_BP_Post_PTA	100.0%	100.0%	100.0%

 $Table \ (13) \ \text{bleeding}$

			Bleeding		
			Yes	No	Total
Side	Right	Count	1	19	20
		% within Bleeding	100.0%	65.5%	66.7%
	Left	Count	0	10	10
		% within Bleeding	.0%	34.5%	33.3%
Total		Count	1	29	30
		% within Bleeding	100.0%	100.0%	100.0%

 $Table \ (14) \ \text{mortality}$

			Death		
			Yes	No	Total
Side	Right	Count	1	19	20
		% within Death	100.0%	67.9%	69.0%
	Left	Count	0	9	9
		% within Death	.0%	32.1%	31.0%
Total		Count	1	28	29
		% within Death	100.0%	100.0%	100.0%

30 days follow-up period

	_		@30_Days_Follow_Up		
			Yes	No	Total
Side	Right	Count	19	1	20
		% within @30_Days_Follow_Up	65.5%	100.0%	66.7%

	Left	Count	10	0	10
		% within @30_Days_Follow_Up	34.5%	.0%	33.3%
Total		Count	29	1	30
		% within @30_Days_Follow_Up	100.0%	100.0%	100.0%

Discussion.

Carotid artery stenting has been recently introduced as an alternative revascularization modality in high-risk patients [12]. It is well established that the presence of carotid artery stenosis is a significant predictor of poor outcomes in patients undergoing coronary bypass graft surgery (CABG) [6]. Current guidelines state that carotid artery stenting is probably recommended before CABG or concomitant to CABG in patients with symptomatic carotid stenosis or in asymptomatic patients with a unilateral or bilateral internal carotid stenosis of 80%.[9]. However, the optimal management of

these patients still remains controversial in clinical practice [13].

The stent procedures were performed in the initial phase of the development of this new revascularization alternative with a significant proportion of interventions performed without distal protection [14]. Although it appears clear that operator experience and the use of distal protection devices are important factors of procedural success, the incidence of stroke associated with the stent intervention in the current analysis was 4.0% and the incidence of death and any stroke was 4.7%, results that are similar or even lower than the currently reported complications [13]. Actually this was the stimulus for this current study to investigate the outcome and the incidence of complication that could be occurred in this situation. Our current study showed that all patients were discharged home at a mean of 6 days postoperatively while CABG was done on the same day.

On the other hand the time interval between CAS, following hospital discharge, and

CABG varied among different studies with a mean of 32 days (range, 2 to 157 days)

[15,16]. The study with the shortest mean waiting period was 15 days and the longest

69 days. During this period, a total of 6 (2.2%) patients died. All deaths were

considered cardiac-related events [17,18].

In the current study tirofeben infusion was started one hour before stenting procedure and was maintained for 4 hours after, then discontinued 2 hours before surgery. Although there was only one case of suspecting bleeding in this study, the balance between the bleeding/thrombotic risk associated with CAS and the risk for a coronary event while waiting for surgery is difficult to determine and, to date, there is no clear consensus on the optimal management of these patients. Some groups have proposed performing CABG on the same day after successful CAS using only aspirin and heparin and to start clopidogrel immediately after CABG[18]. Others have proposed the use of short-acting glycoprotein IIb/IIIa inhibitors during CAS and performing CABG 4 to 6 hours after stenting [19].

One patient in our study suffered some drop of blood pressure following stenting of RICA, prior to surgery. However, this patient had CABG surgery after stabilization of the blood pressure with no complications postoperatively. Systemic hypotension produced by stimulation of the carotid baroreceptor may occur in patients undergoing CAS. The duration of hypotension can be as long as several days to weeks and may have played a role in impairing myocardial perfusion in this high-risk group of patients with advanced coronary artery disease [20]. Thus, this may have contributed, at least in part, to the occurrence of cardiac events during the waiting period in this analysis. Prevention of cerebrovascular events is the main goal of performing carotid revascularization before CABG .This suggests that close clinical and hemodynamic monitoring may be critical after successful CAS to reduce the risk of cardiac complications while waiting for CABG. The present study showed that after successful carotid revascularization, the incidence of any stroke after CABG was nil although this incidence appears to be excellent results and encouraging, the overall incidence of any stroke combining both carotid and coronary revascularization procedures in other study was 6.0% with an incidence of major stroke of 3.2% [21]. On the other hand it is difficult to predict if the incidence of stroke would have been lower if carotid revascularization would have not been performed, the overall incidence found in this analysis appears to be similar to prior reports in patients with carotid stenosis without revascularization [22,23]. This emphasizes the concept that the presence of carotid stenosis is probably a marker of more advanced atherosclerotic disease and of high risk. Unfortunately there are no prospective data regarding outcomes in patients with combined coronary and carotid stenosis. Using a casecontrol study, Ricotta et al. also found an increased incidence of stroke and death in patients undergoing the simultaneous CEA and CABG surgery approach, but they concluded that the increased risk was probably because of the increased atherosclerotic burden in that group rather than the added surgical procedure.[24]. Agel R, and co-workers reported a combined rate of stroke and mortality of 13.0% with the joint procedure compared with 4.9% for CABG surgery alone.[25]. Of note, no study has shown the superiority of the combined procedure over the two-staged approach. Our results slightly different to that reported by Tanimoto et al 2005 ., about the prevalence of severe carotid disease (>70%) in those with three vessel or left main coronary disease which could be related to environmental and genetic factors [26]. Our results go with that reported by Polydorou A. D et al., 2010 but in asymptomatic patients with internal carotid artery lesions of >80%, were reduced by CAS to <20% in all cases, achieving a procedural success of 100%. There were no neurological complications, such as TIA and stroke, or death. The difference in that study was the follow up which extended to 12 months and one patient developed acute coronary syndrome one day after CAS and was treated accordingly [20]. Regarding mortality in the current study .there was only one patient, who had a RICA stent prior to a concomitant surgery for aortic valve replacement and CABG but he did not survived during the follow-up period and passed 2 days postoperatively due to intractable arrythmias.

Conclusion.

With the aging CABG population, the presence of concurrent severe carotid disease is a matter of serious concern. The best revascularization strategy for patients with advanced coronary and carotid disease should be suggested on a case-by-case basis by a multidisciplinary team that includes neurologists, surgeons, and interventionists who take into account the co-morbidities of the patient, the degree of urgency of cardiac surgery, and local expertise. Prospective, randomized studies are warranted to fully elucidate the best therapeutic approach in this growing patient population. However, and despite the limited number of patients in our study, carotid artery stenting can be considered a safe procedure and less invasive than surgical endarterectomy for management of patients with combined carotid and coronary artery disease.

Several questions with regard to management in this setting remain unanswered in the absence of large randomized clinical trials. Prospective, randomized studies are warranted to fully elucidate the best therapeutic approach in this growing patient population.

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